Dissertation on

"STROKE VOLUME VARIATION AS A PREDICTOR FOR FLUID RESPONSIVENESS IN PATIENTS UNDERGOING ELECTIVE MAJOR ABDOMINAL SURGERIES"

Submitted to the

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

in partial fulfilment of the requirements
for the award of degree of

M.D. (Branch-X)

ANAESTHESIOLOGY

GOVERNMENT STANLEY MEDICAL COLLEGE & HOSPITAL

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY,

CHENNAI, TAMILNADU

APRIL 2012

DECLARATION

I, **DR.K.J.KAVIYA**, Solemnly declare that the dissertation, titled **"STROKE VOLUME VARIATION AS A PREDICTOR FOR FLUID RESPONSIVENESS IN PATIENTS UNDERGOING ELECTIVE MAJOR ABDOMINAL SURGERIES",** is a bonafide work done by me during the period of February 2011 to June 2011 at Government Stanley Medical College and Hospital, Chennai under the expert guidance and supervision of **Dr. P. CHANDRASEKAR, M.D. D.A.,** Professor and Head, Department Of Anaesthesiology, Government Stanley Medical College, Chennai. This thesis is submitted to The Tamil Nadu Dr. M.G.R. Medical University in partial fulfilment of the rules and regulations for the M.D. degree examinations in Anaesthesiology to be held in April 2012.

Chennai-1 **DR.K.J.KAVIYA**

Date:

CERTIFICATE

This is to certify that the dissertation entitled "**STROKE VOLUME VARIATION AS A PREDICTOR FOR FLUID RESPONSIVENESS IN PATIENTS UNDERGOING ELECTIVE MAJOR ABDOMINAL SURGERIES**" is a genuine work done by **Dr. K.J.KAVIYA** for the partial fulfilment of the requirements for M.D. (Anaesthesiology) Examination of The Tamilnadu Dr. M.G.R. Medical University to be held in April 2012, under my supervision and the guidance of **Dr. MADAN KUMAR M.D. D.A.,** Professor, Department of Anaesthesiology at Stanley Medical College, Chennai.

Prof. Dr. MADAN KUMAR,
M.D., D.A.,
Professor,
Department of Anaesthesiology,
Govt. Stanley Medical College and Hospital,
Chennai – 600 001.

Prof. Dr. P. CHANDRASEKAR,
M.D., D.A.,
Professor and H.O.D.
Department of Anaesthesiology
Govt. Stanley Medical College and Hospital, Chennai – 600 001.

Dr. GEETHA LAKSHMI, M.D.,PhD
Dean
Govt. Stanley Medical College,
Chennai – 600 001.

ACKNOWLEDGEMENTS

I wish to express my sincere thanks to **Prof. Dr. GEETHA LAKSHMI M.D.,PhD,** Dean, Government Stanley Medical College and Hospital for having permitted me to utilize the facilities of the hospital for the conduct of the study.

My heartfelt gratitude to **Prof. Dr. P. CHANDRASEKAR M.D., D.A.,** Professor and Head, Department of Anaesthesiology, Government Stanley Medical College and Hospital for his motivation, valuable suggestions, constant supervision and for all necessary arrangements for conducting this study.

I am greatly indebted **to Prof. Dr. R.MATHAN KUMAR, M.D., D.A.,** and **Prof. Dr. N. KRISHNAN M.D. D.A.,** who guided me throughout the study and offered constructive criticism and suggestions throughout the period of the study.

I thank **Prof. Dr. PONNAMBALAM NAMASIVAYAM, M.D., D.A., Prof. Dr. R. LAKSHMI, M.D., D.A.,** for their constant encouragement and support.

I express my heartfelt gratitude to Assistant Professors **Dr. SATISH LOGIDASAN, M.D., D.N.B., Dr. DEEPTI, M.D.,** who had evinced constant and keen interest in the progress of my study right from the inception till the very end and were instrumental in the successful completion of the study.

I wish to thank all my Assistant Professors especially **Dr.GAYATHRI D.A., M.D., Dr. KANIMOZHI M.D.,** for their aid and encouragement during the study.

I thank **Mr. A. ALBERT JOSEPH** for guiding me in statistical analysis.

My sincere thanks to all those post graduates who helped me during this study period.

I thank the staff nurses and theatre personnel, Government Stanley Medical Hospital for their cooperation and assistance.

I owe my gratitude to all the patients included in the study and their relatives, for their whole hearted co-operation and consent.

CONTENT

INTRODUCTION

Fluid loading[3] is one of the most common therapeutic intervention in patients undergoing surgery, as well as in patients with hypotension[39] or shock. It is very challenging to determine which level of preload is optimal in an "abnormal" situation (eg, vasodilation induced by anesthetic agents or sepsis). Therefore, to determine fluid therapy, a very practical approach consists in detecting patients who will be able to turn fluid loading into a significant increase in stroke volume (SV) and cardiac output (CO) .Clinical end points of fluid therapy are sometimes different i.e. increasing blood pressure, or urine output but will be achieved only if the physiologic effect an increase in stroke volume .If not, fluid administration is useless or even potentially harmful as in worsening pulmonary and tissue edema, hemodilution. Therefore reliable sensitive and specific indicators of fluid responsiveness which recognize the ability to turn fluid loading into a significant increase in Stroke volume (SV) are needed.

Conventional hemodynamic variables, such as blood pressure, heart rate (HR), central venous pressure (CVP)[38], and even pulmonary artery occlusion pressure (PAOP)[22], are insensitive and sometimes misleading in the assessment of circulating blood volume. As an

alternative to these static variables, assessment of stroke volume variation (SVV)[27] has been used as a dynamic index to guide fluid therapy. Mechanical ventilation induces cyclic variations in venous return which may be turned into cyclic variations in SV (SVV). Stroke volume variation may be used as a continuous preload variable that allows for optimal fluid management. The SVV are more pronounced during hypovolemia and the variation decreases if intravascular volume is restored.SVV has shown to reliably predict changes in cardiac output.

Hence a prospective observational study was done to compare the effects of fluid responsiveness on Stroke volume variation and central venous pressure and also to determine which variable reliably predicts fluid responsiveness.

AIM OF THE STUDY

The aim of this study was to assess whether Stroke volume variation(SVV) can serve as a predictor of fluid responsiveness in patients undergoing elective major abdominal surgery.

To compare Stroke volume variation (SVV) with Central venous pressure (CVP) for fluid responsiveness.

PRELOAD VARIABLES

Preload is best defined as left ventricular end-diastolic volume (LVEDV). According to the Frank–Starling principle as the preload increases left ventricular stroke volume increases until the optimal preload is achieved at which point the stroke volume remains relatively constant (see Figure 1). This optimal preload is related to the maximal overlap of the actin-myosin myofibrils. It is important to note that in an intact heart the actin-myosin links cannot be disengaged and hence there is *no descending limb* of the Frank–Starling curve. Once the left ventricle is functioning near the 'flat' part of the Frank–Starling curve fluid loading has little effect on cardiac output and only serves to increase tissue edema and to promote tissue hypoxia. In normal physiologic conditions, both ventricles operate on the ascending portion of the Frank–Starling curve[5]. This mechanism provides a functional reserve to the heart in situations of acute stress.

In normal individuals, an increase in preload (with volume challenge) results in a significant increase in stroke volume[37]. In contrast, only about 50% of patients with circulatory failure will respond to a fluid challenge[31]. Furthermore, as a result of altered left ventricular compliance and function, the position of an acutely ill patient on the Frank–Starling

curve cannot be predicted from their preload (LVEDV) alone. In critically ill patients it is therefore important not only to determine the patients' preload (LVEDV) but their fluid responsiveness, i.e. to whether the patient will

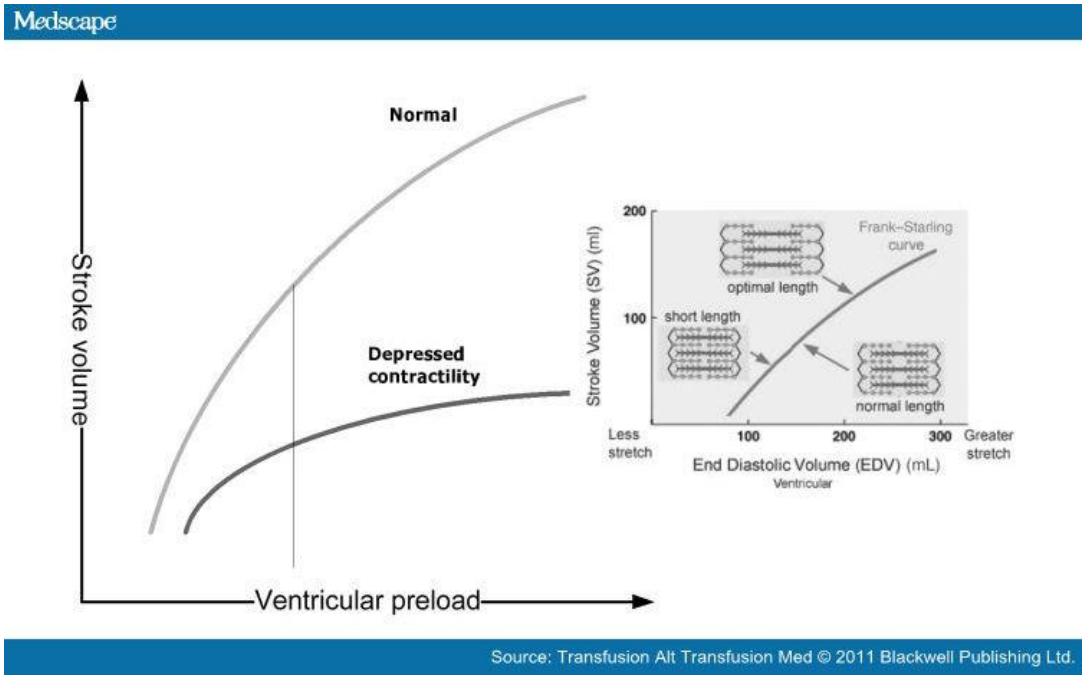


FIG 1: Frank starling Curve

Have an increase in stroke volume or cardiac output with fluid loading (i.e. have recruitable cardiac output). Simultaneously, it is important to determine the patients' overall fluid balance and more specifically the interstitial fluid volume. In patients with increased interstitial fluid volume it is more appropriate to increase cardiac output by using a vasoactive agent rather than with fluid boluses alone. Volume

responsiveness may be defined as increased systolic volume (SV) with consequent increased cardiac output (CO) from an established volume infusion which would provide better oxygen supply to the tissue.

However,this response to volume testing will only take place when both ventricles operate in the ascending phase of the Frank-Starling curve, i.e., in a preload dependence status.

STROKE VOLUME VARIATION:

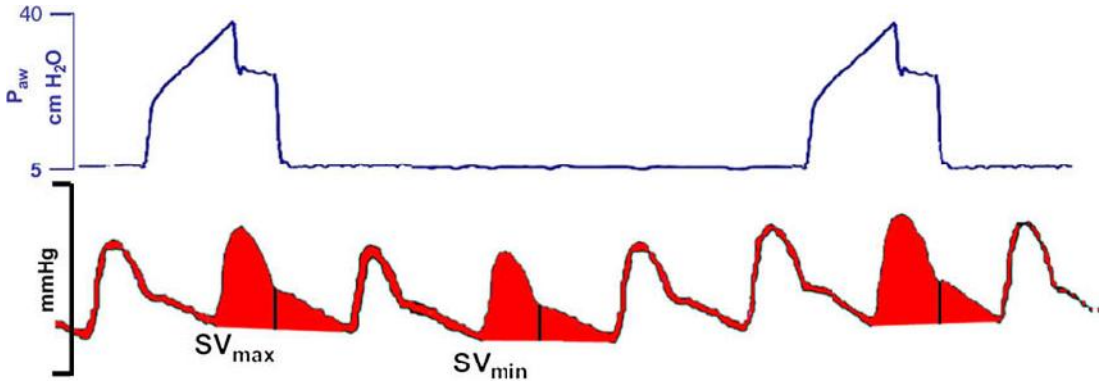


FIG 2 : The respiratory-cycle-induced changes in stroke volume (SV).

The stroke volume variation is calculated between the maximal (SVmax) and minimal (SVmin) values of stroke volume. Paw, positive airway pressure.

Physiological basis for heart–lung interactions

Heart–lung interactions[30] can be understood based on the effects of changes in intrathoracic pressure (ITP) and lung volume on venous return and left ventricular ejection, and the energy needed to create these changes. During spontaneous ventilation, venous return increases with negative swings in ITP, subsequently increasing right ventricular volume and causing the intraventricular septum to move into the left ventricle. This is manifested by a spontaneous inspiration-associated decrease in left ventricular end-diastolic volume and decreased left ventricular diastolic compliance. This decreased left ventricular preload causes an immediate decrease in left ventricular stroke volume and pulse pressure which is referred to as pulsus paradoxus. The more vigorous the ventilatory efforts, the greater the ITP swings and the more pulsus paradoxus occurs.

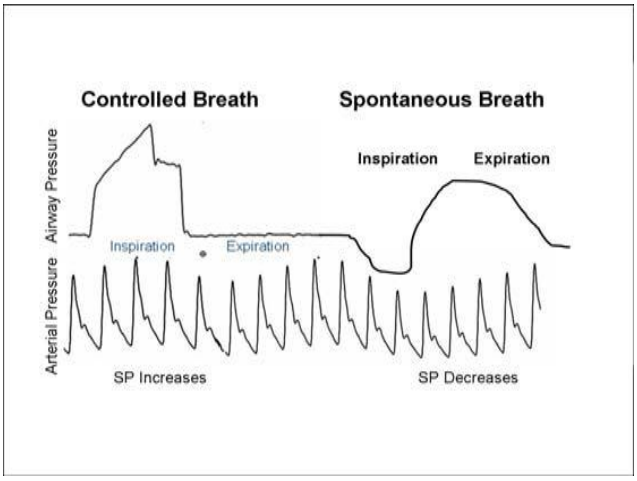


Fig 3: Variation during spontaneous and controlled ventilation

Until recently it was felt that ventricular interdependence was minimal during normal tidal volume positive-pressure ventilation because the changes in ITP are small, making both the lung inflation-induced pulmonary vascular resistance and venous return changes small. Mitchell et al.[32], however, showed in dogs that positive-pressure ventilation also altered left ventricular output in a fashion explained by ventricular interdependence.

The principles underling the SVV are based on simple physiology[32]. Intermittent positive pressure ventilation induces cyclic changes in the loading conditions of the left and right ventricles. Mechanical insufflation decreases preload and increases after load of the RV. The RV preload reduction is due to the decrease in the venous return pressure gradient that is related in the inspiratory increase in pleural pressure. The increase in RV afterload is related to the inspiratory increase in transpulmonary pressure. The reduction in RV preload and increase in RV afterload both lead to a decrease in RV stroke volume, which is at a minimum at the end of the inspiratory period.

The inspiratory reduction in RV ejection leads to a decrease in LV filling after a phase lag of two or three heart beats because of the long blood pulmonary transit time. Thus the LV preload reduction may induce a decrease in LV stroke volume, which is at its minimum during the

expiratory period. The cyclic changes in RV and LV stroke volume are greater when the ventricles operate on the steep rather than the flat portion of the Frank–Starling curve .Therefore, the magnitude of the respiratory changes in LV stroke volume is an indicator of biventricular preload dependence. So in a mechanically ventilated patient, positive pressure ventilation displaces the ventricle wall inward during systole to assist in ventricular emptying causing a slight rise in the systolic pressure during mechanical inspiration. This is called the reverse pulsus paradoxus which is a sensitive indicator of hypovolaemia.

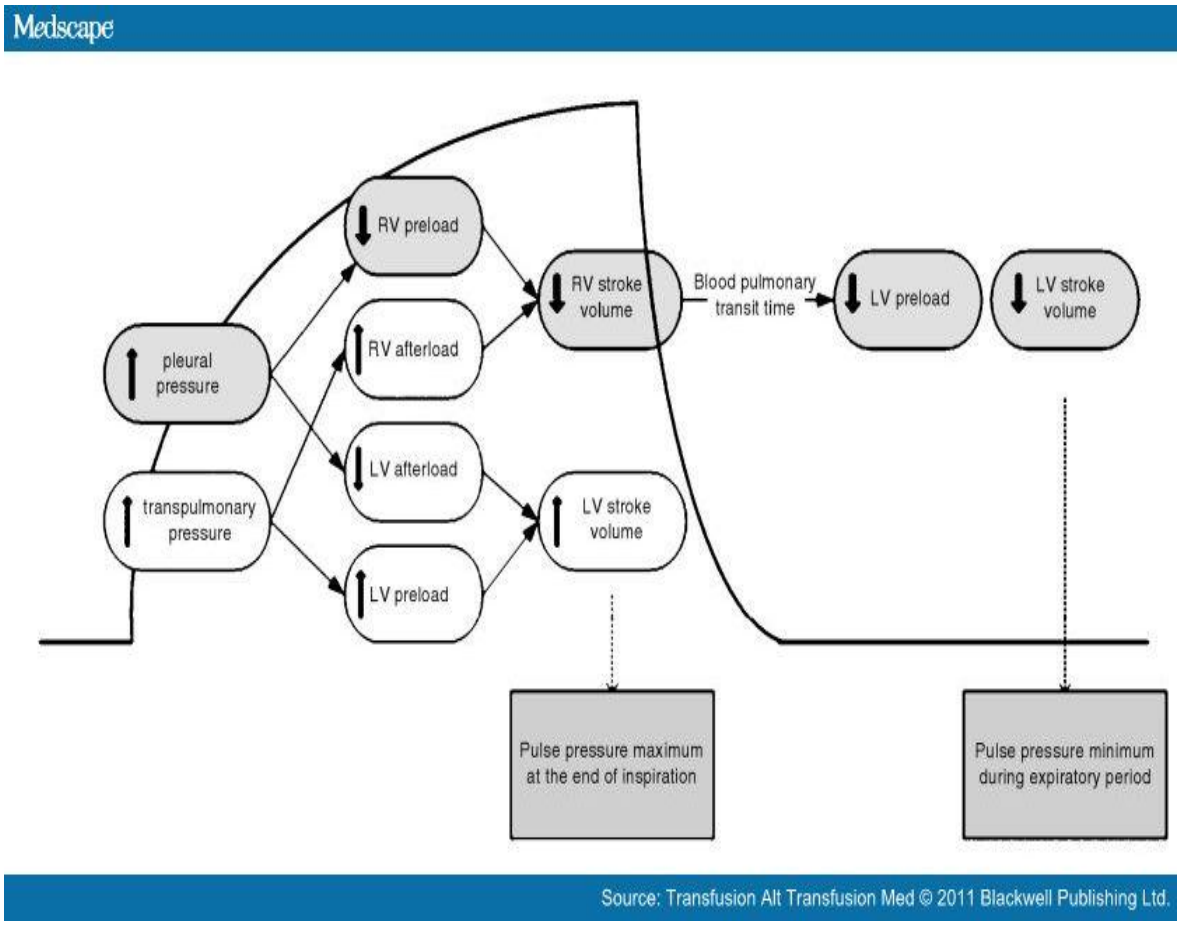


Fig 4: Physiology of stroke volume variation.

The enormous appeal of using the *SVV as a marker of volume responsiveness is that it dynamically predicts an individual patients' position on their Starling curve and this is independent of ventricular function and compliance as well as pulmonary pressures* and mechanics unlike the central venous pressure. Furthermore, this technology is relatively simple both in concept and in execution and is conducive to monitoring both in the operating room and ICU. It should be appreciated that both arrhythmias and spontaneous breathing activity[40] will lead to misinterpretations of the respiratory variations in pulse pressure/stroke volume. Furthermore, for any specific preload condition the SVV will vary according to the tidalvolume[(28,34)].The normal values of SVV is less than 10 -15 % in mechanically ventilated patients with different studies quoting a different threshold range.

Reuter[30] and colleagues demonstrated a linear relationship between tidal volume and SVV. De Backer[29] and colleagues evaluated the influence of tidal volume on the ability of the PPV to predict fluid responsiveness. These authors reported that the SVV was a reliable predictor of fluid responsiveness only when the tidal volume was at least 8 mL/kg

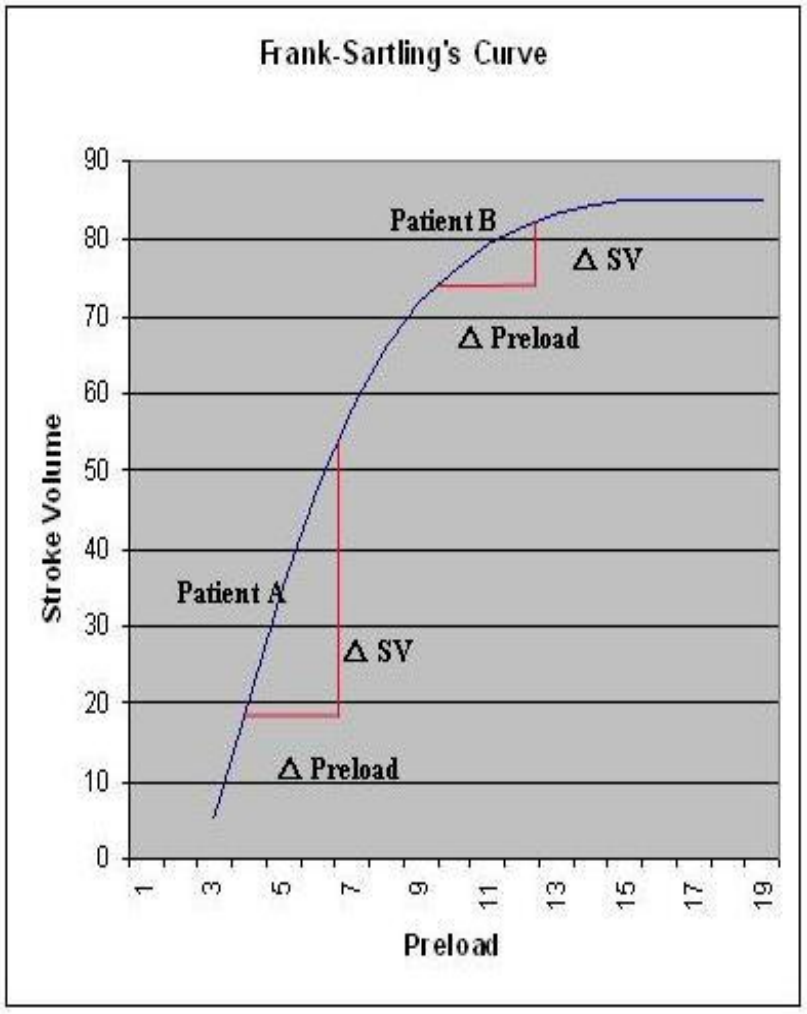


Fig 5: Volume challenge

- Patient A is preload responsive:

  On steep part or fluid responsive portion

  Fluid bolus results in significant increase in SV

- Patient B is not preload responsive:

  On plateau portion of curve; No preload recruitibility

  Same bolus volume does not result in significant increase in SV

The time-honored method of assessing preload responsiveness is to administer a relatively small intravascular volume bolus rapidly and observe the subsequent hemodynamic response in terms of blood pressure, pulse, cardiac output, SvO_2 and related measures. There is little agreement regarding what absolute volume and infusion rate defines an adequate fluid challenge. In a volume challenge trial estimates of improved circulatory status (e.g. increasing blood pressure and decreasing heart rate) and improved effective blood flow (e.g. increasing SvO_2 and decreasing blood lactate) are used to document a beneficial response[47]. The primary factor addressed by a fluid challenge is preload responsiveness; specifically, will cardiac output increase with fluid loading? Thus, a fluid challenge must be conducted within the context of known or suspected tissue hypoperfusion. Furthermore, a volume challenge is not fluid resuscitation; it is merely a test to identify those who are preload responsive. Volume responders can then be given additional fluid resuscitation with minimal risk for worsening cor pulmonale or inducing pulmonary edema.

A minimally invasive hemodynamic monitoring technology has been developed for the analysis of the arterial pressure wave to determine cardiac output. This is classified as Pulse Contour analysis or Pulse

Pressure Analysis[24]. Devices are now available on the market, with different algorithms and features:

- Flotrac technology and Vigileo Monitor[25] (Edwards Lifesciences, Irvine, CA, USA)is one among them.

Physics and Physiology

Flow is determined by a pressure gradient along a vessel and the resistance to that flow ($F=\Delta P/R$). The FloTrac algorithm uses a similar principle to measure pulsatile flow by incorporating the effects of both vascular resistance and compliance through a conversion factor known as Khi (χ).

Cardiac output is calculated by multiplying heart rate by the stroke volume. The FloTrac algorithm uses these same components but substitutes heart rate with the pulse rate (PR), capturing only truly perfused beats, and multiplies PR by a calculated stroke volume. Stroke volume is calculated from the patient's arterial pressure using a specially designed system, the FloTrac sensor.

The FloTrac algorithm analyzes the pressure waveform at one hundred times per second over 20 seconds, capturing 2,000 data points for analysis. These data points are used along with patient demographic information to calculate the standard deviation of the arterial pressure

(σAP). This (σAP) is proportional to pulse pressure (PP). The σAP is multiplied by a conversion factor known as Khi (χ) which incorporates both the effects of resistance and compliance (vascular tone) and also converts σAP in (mmHg) into ml/beat. Therefore, with the variables σAP and vascular tone (χ) flow or stroke volume can be calculated.

Fig 6: VIGILEO MONITOR WITH FLOTRAC TRANSDUCER.

Traditional: CO = HR * SV

FloTrac system: APCO –Arterial pressure based cardiac output:

APCO= PR x (σAP * χ)

Where χ = M (HR, σAP, C(P), BSA, MAP, µ3ap, µ4ap . . .)

σAP = standard deviation of arterial pulse pressure in mmHg is proportional to pulse pressure.

χ = scaling multivariate parameter proportional to the effects of vascular tone on pulse pressure.

M = multivariate polynomial equation.

BSA =body surface area calculated by Dubois' equation for body surface area.

MAP = mean arterial pressure calculated by taking sum of sampled pressure point values over 20 seconds and dividing it by the number of pressure points.

μ = statistical moments determined by skewness(symmetry) and kurtosis (distinctness of a peak)calculated along several mathematical derivatives.

SVV is calculated as the variation of the beat-to beat SV from the mean value during the most recent 20 seconds:

SVV = SVmax _ SVmin /SVmean

where SVmax is the maximum stroke volume,

SVmin is the minimum stroke volume

SVmean is the mean stroke volume

Since clinically available, the FloTrac system has been validated against various cardiac output technologies including thermodilution cardiac output.

No Manual Calibration Needed:

Since the FloTrac algorithm continuously adjusts for the patient's ever changing vascular tone, it does not require manual calibration. As a component of the calibration, Khi auto corrects for changes in vascular tone through a complex waveform analysis.

Technical Considerations

The algorithm is dependent upon a high fidelity pressure tracing. Attention to best practice in pressure monitoring is important by; priming with gravity, pressure bag kept to 300mmHg, adequate I.V. bag flush volume, sensor stopcock is kept level to phlebostatic axis, and periodic testing of optimal dampening with a square wave

FloTrac sensor is only indicated for adult use and has not been validated in patients with ventricular assist devices or intra aortic balloon pumps. Absolute values during aortic regurgitation may be affected although trending may be appropriate. Severe peripheral constriction during shock states or hypothermic episodes may influence values with radial arterial locations, consideration to femoral sites during these episodes or insertion of a pulmonary artery catheter may be considered.

The ease of use of this system allows for earlier implementation of flow monitoring in patients. The system is minimally invasive, easy-to-use and allows for the continuous monitoring of essential hemodynamic information such as Continuous cardiac output CCO, Stroke volume SV, Stroke volume variation SVV, Systemic vascular resistance SVR.

Central venous pressure:

Venous pressure is a term that represents the average blood pressure within the venous compartment. The term "central venous pressure" (CVP)[34] describes the pressure in the thoracic vena cava near the right atrium. CVP is a major determinant of the filling pressure and therefore the preload of the right ventricle, which regulates stroke volume through the Frank-Starling mechanism.

A change in CVP (ΔCVP) is determined by the change in volume (ΔV) of blood within the thoracic veins divided by the compliance (Cv) of the these veins according to the following equation:

$$\Delta CVP = \Delta V / Cv$$

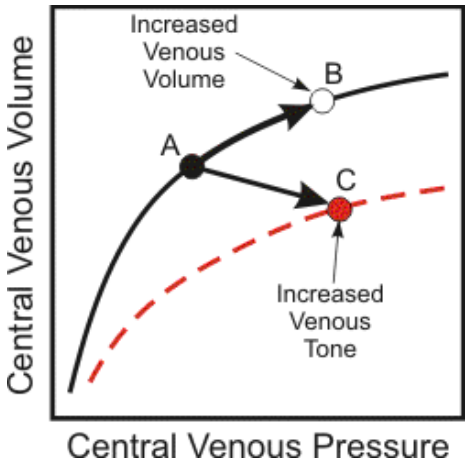


Fig 7:The effects of increased venous blood volume and decreased venous compliance on CVP.

Therefore, CVP is increased by either an increase in venous blood volume or by a decrease in venous compliance. The latter change can be caused by contraction of the smooth muscle within the veins, which increases the venous vascular tone and decreases compliance. In figure 4 , point A represents a control operating point for the venous vasculature. The curve that point A is on is the compliance curve for the thoracic veins. If the volume of blood within these veins is increased, then the operating point will shift up and to the right (from A to B) along the same compliance curve. This will lead to an increase in pressure that is determined by the change in volume and the venous compliance (slope of the curve). CVP will also be increased if venous smooth muscle contraction is enhanced i.e.., by sympathetic nerve stimulation). When this occurs, the venous compliance decreases (dashed line), and the new

operating point C will reflect a smaller venous volume but at a greater venous pressure.

It is important to note that the compliance of the large thoracic veins (especially the vena cava) does not undergo large changes. Instead, the major site for venous compliance changes is smaller veins located outside of the thorax. These smaller veins are can undergo significant compliance changes. When the compliance of these veins decreases (e.g., by sympathetic nerve stimulation), constriction of these veins and the resulting increased pressure is transmitted up to the thoracic veins, which increases their volume and therefore pressure.

Factors affecting the measured CVP[40]:

- Central venous blood volume
  - _ Venous return/cardiac output
  - _ Total blood volume
  - _ Regional vascular tone
- Compliance of central compartment
  - _ Vascular tone
  - _ RV compliance
  - _ Myocardial disease
  - _ Pericardial disease
  - _ Tamponade

- Tricuspid valve disease
  - _ Stenosis
  - _ Regurgitation
- Cardiac rhythm
  - _ Junctional rhythm
  - _ Atrial fibrillation (AF)
  - _ Atrio ventricular (A-V) dissociation
- Reference level of transducer
  - _ Positioning of patient
- Intrathoracic pressure
  - _ Respiration
  - _ IPPV
  - _ Positive end-expiratory pressure (PEEP)
  - _ Tension pneumothorax

The central venous pressure (CVP) is frequently used to guide fluid management. The basis for using the CVP to guide fluid management comes from the dogma that the CVP reflects intravascular volume; specifically it is widely believed that patients with a low CVP are volume depleted while patients with a high CVP are volume overloaded. Furthermore, the '5-2' rule that was popularized in the 1970's is still widely used today for guiding fluid therapy. According to this rule, the

change in CVP following a fluid challenge is used to guide subsequent fluid management decisions.

The CVP is a good approximation of right atrial pressure, which is a major determinant of right ventricular filling. It has therefore been assumed that the CVP is a good indicator of right ventricular preload. Furthermore, as right ventricular stroke volume determines left ventricular filling, the CVP is assumed to be an indirect measure of left ventricular preload. However, because of the changes in venous tone, intrathoracic pressures (positive end expiratory pressure, etc.), there is a poor relationship between the CVP and right ventricular end-diastolic volume. Furthermore, the right ventricular end-diastolic volume may not reflect the patients' position on the Frank–Starling curve and therefore preload reserve.

Recently, the idea that the CVP reflects blood volume has been challenged. CVP is only a very small part of venous return/cardiac output

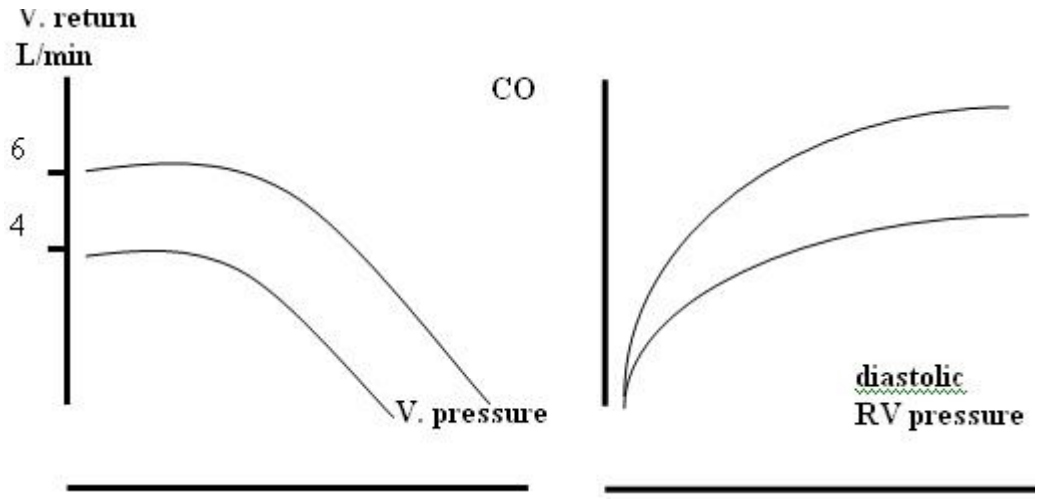
• Venous Return (VR) = Mean Circulatory Filling Pressure – C*VP/* Venous Resistance

• CVP measured is intramural, but desired value is *transmural* pressure

Interpretation of the CVP

The following discussion is designed to assist in the interpretation of the CVP when the measurement of the CO is not available.

Venous return and **CO** are described by these two curves:



The Fig 8 shows two venous return curves: the upper represents a normal circulating volume (CO = 6 L/min) and the lower represents hypovolemia. The diagram on the right shows two contractility ('Starling') curves, the lower one representing a decreased contractility. At steady state, venous return and CO are equal, and the two curves can be constructed on the same graph. **The point at which the two curves intersect is the CVP**.

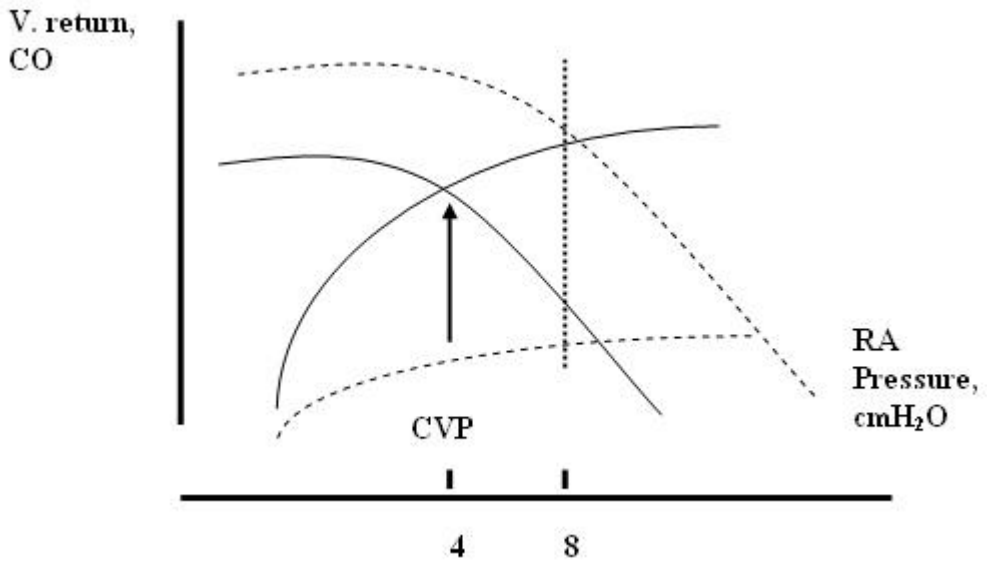


Fig 9: Intersecting CVP curves.

In the above graph Fig 9., the starting CVP is 4 cmH_2O. If the CVP increases to 8 cmH_2O, the new value can occur at a variety of CO values, as shown by the dotted vertical line, with different physiological implications. The two possible extremes are that the CVP has increased only due to an increase in volume (new venous return curve) or that it has increased only due to a decrease in contractility (new Starling curve). Clearly, a combination of both phenomena is possible. The same thinking process can be illustrated for a decrease in CVP. Hence, an isolated CVP value can represent very different hemodynamic conditions, and without a CO measurement, it is difficult to interpret the change in CVP. In a reasonably stable patient, changes in MAP should parallel changes in CO. An increase in CVP will be likely due to an increased circulating volume if the MAP also increases. An increase in CVP will

be likely due to a decreased contractility if the MAP decreases. In an unstable patient, measurement of the CO may be necessary.

Limitations of CVP Monitoring

- Not a measure of circulating blood volume
  - The body attempts to maintain homeostasis (adequate transmural CVP)
  - Mean circulating filling pressure is a better measure (but difficult to determine)
- CVP is a static hemodynamic variable
- CVP affected by *many* other variables as already discussed.

Receiver operating characteristic (**ROC**)[29], or simply **ROC curve**, is a graphical plot of the sensitivity, or true positive rate, vs. false positive rate (1 − specificity or 1 − true negative rate).The ROC can also be represented equivalently by plotting the fraction of true positives out of the positives (TPR = true positive rate) vs. the fraction of false positives out of the negatives (FPR = false positive rate).Also known as a Relative Operating Characteristic curve, because it is a comparison of two operating characteristics (TPR & FPR) as the criterion changes.

Consider a diagnostic test that seeks to determine whether a person has a certain disease. A false positive in this case occurs when the person tests positive, but actually does not have the disease. A false negative, on the other hand, occurs when the person tests negative, suggesting they are healthy, when they actually do have the disease.

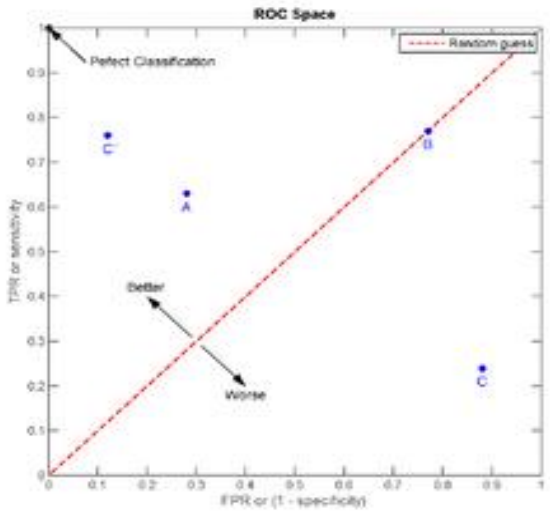


Fig 10: Receptor operator characteristic curves.

To draw an ROC curve, only the true positive rate (TPR) and false positive rate (FPR) are needed. TPR determines a classifier or a diagnostic test performance on classifying positive instances correctly among all positive samples available during the test. FPR, on the other hand, defines how many incorrect positive results occur among all negative samples available during the test.

A ROC space is defined by FPR and TPR as *x* and *y* axes respectively, which depicts relative trade-offs between true positive (benefits) and false positive (costs). Since TPR is equivalent with sensitivity and FPR is equal to 1 − specificity, the ROC graph is sometimes called the sensitivity vs (1 − specificity) plot. The best possible prediction method would yield a point in the upper left corner or coordinate (0,1) of the ROC space, representing 100% sensitivity (no false negatives) and 100% specificity (no false positives). The (0,1) point is also called a *perfect classification*. The diagonal divides the ROC space. Points above the diagonal represent good classification results, points below the line poor results. Area Under Curve (AUC) is equal to the probability that a classifier will rank a randomly chosen positive instance higher than a randomly chosen negative one. It can be shown that the area under the ROC curve is closely related to the Mann–Whitney U which tests whether positives are ranked higher than negatives. A reliable and valid AUC estimate can be interpreted as the probability that the classifier will assign a higher score to a randomly chosen positive example than to a randomly chosen negative example.

REVIEW OF LITERATURE

Cardiac preload is one determinant of cardiac output (CO). Optimizing cardiac preload is therefore crucial in the care of hemodynamically unstable patients. Numerous parameters for assessing cardiac preload and guiding fluid therapy have been suggested and extensively studied. Over the last decade, functional preload parameters such as stroke volume variation (SVV) and others have been repeatedly described to be superior when compared with cardiac filling pressures central venous pressure (CVP) and pulmonary artery occlusion pressure. An extensively studied method for monitoring functional preload is the pulse contour derived SVV. Its feasibility and appropriateness in estimating cardiac preload and volume responsiveness has been reported in many clinical trials.

Zimmermann et al (EJA 2010)[49]compared the accuracy of arterial pressure-based stroke volume variation (SVV) with central venous pressure to predict the response of stroke volume index(SVI) to volume replacement in patients undergoing major abdominal surgery. They studied 20 patients scheduled for elective major abdominal surgery. After induction of anaesthesia, all haemodynamic variables were recorded immediately before and subsequent to volume replacement by infusion

of 6% hydroxy-ethyl starch (HES) 130/0.4 (7 ml kg) at a rate of 1 ml kg min. The volume-induced increase in SVI was at least 15% in 15 patients (responders) and less than 15% in five patients (nonresponders). Baseline SVV correlated significantly with changes in SVI (DeltaSVI; r = 0.80; P < 0.001) as, whereas baseline values of central venous pressure showed no correlation to DeltaSVI and concluded that SVV can serve as valid indicators of fluid responsiveness in mechanically ventilated patients undergoing major abdominal surgery.

Derichard A, Robin E, et al (BJA 2009)[13] compared the ability of two algorithms automated calculation of PPV (PPV(auto)) (Intellivue MP 70) and stroke volume variation (SVV(auto)) (FloTrac/Vigileo) to predict fluid responsiveness during abdominal surgery. 56 fluid challenges given for haemodynamic instability in 11 patients undergoing major abdominal surgery. Fluid responsiveness was defined as an increase in stroke volume index (SVI) >10%. PPV(ref), PPV(auto), SVV(auto), and SVI were recorded simultaneously before and after each fluid challenge. The authors concluded that PPV(auto) and SVV(auto) predict fluid responsiveness accurately in patients with haemodynamic instability during major abdominal surgery.

Haim Berkenstadt, MD, Nevo Margalit, MD et al(Anesthesia analgesia 2001)[3] Studied stroke volume variation (SVV) as a predictor of fluid responsiveness. Fifteen patients undergoing brain surgery were included. During surgery, graded volume loading was performed, with each volume loading step (VLS) consisting of 100 mL of 6% hydroxyethylstarch given for 2 min. A total of 140 VLSs were performed. The author concluded that Responsive and non responsive VLSs differed in their pre-VLS values of systolic blood pressure, SV, and SVV, but not in the values of heart rate and central venous pressure. An SVV value of 9.5% or more, will predict an increase in the SV of at least 5% in response to a 100-mL volume load, with a sensitivity of 79% and a specificity of 93%.

Marik PE, Cavallazzi R, Vasu T, Hirani A. Et al (Critical care medicine 2009)[27] **conducted** a systematic review of the literature to determine the ability of dynamic changes in arterial waveform-derived variables to predict fluid responsiveness and compare them with static indices of fluid responsiveness. Clinical studies that evaluated the association between stroke volume variation and the change in stroke volume/cardiac index after a fluid or positive end-expiratory pressure challenge were considered. Twenty-nine studies (which enrolled 685 patients) were taken into account. Overall, 56% of patients responded to a

fluid challenge. The pooled correlation coefficients between the baseline pulse pressure variation, stroke volume variation, systolic pressure variation, and the change in stroke/cardiac index were 0.78, 0.72, and 0.72, respectively. The mean threshold values were 11.6 +/- 1.9% for the stroke volume variation. The sensitivity, specificity, and diagnostic odds ratio 0.82, 0.86, and 27.34 for the stroke volume variation, respectively .The authors concluded that the dynamic changes of arterial waveform-derived variables during mechanical ventilation are highly accurate in predicting volume responsiveness in critically ill patients with an accuracy greater than that of traditional static indices of volume responsiveness. This technique, however, was limited to patients who receive controlled ventilation and who are not breathing spontaneously

Micah et al (Internet Journal of Anesthesiology 2010)[35] has compared the stroke volume variation (SVV) , arterial pressure based cardiac output (APCO) with the current accepted methods on cardiac output ,the cardiac output values of continuous thermodilutional method. The central APCO was compared with peripheral APCO. The authors concluded that SVV is a good indicator of the cardiac preload. It is superior to static indicators of cardiac preload. APCO measured from peripheral artery had a high correlation with the central CO and

conventional method for CO measurement, therefore, was able to accurately reflect cardiac output.

Cannesson M, Musard H et al (Anesthesia analgesia 2009)[7] assessed the ability of a novel algorithm for automatic estimation of stroke volume variation (SVV) to predict fluid responsiveness in mechanically ventilated patients(n=25) referred for coronary artery bypass grafting. SVV was continuously displayed by the Vigileo/FloTrac system. SVV and DeltaPP were recorded simultaneously before and after an intravascular volume expansion (VE) (500 mL hetastarch). Responders to VE were defined as patients whose cardiac index obtained using thermodilution increased by more than 15% after VE. The authors concluded that SVV was able to reliably predict fluid responsiveness with a threshold SVV value of 10% allowed discrimination of responders to VE with a sensitivity of 82% and a specificity of 88%.

Biais M, Nouette-Gaulain K, et al (Anesthesia Analgesia 2009)[4] compared stroke volume variation (SVV) assessed from a peripheral artery with the Vigileo/FloTrac system (SVV-FloTrac) with SVV derived close to the heart by aortic Doppler (SVV-Doppler). In Thirty patients undergoing liver transplantation concluded that SVV-FloTrac and SVV-Doppler measurements show acceptable bias and limits of agreement, and

similar performance in terms of fluid responsiveness in patients undergoing liver transplantation.

Hofer CK, Müller SM,et al (Chest 2005)[18] evaluated SVV in cardiac patients for predicting fluid responsiveness in forty patients with preserved left ventricular function undergoing elective off-pump coronary artery bypass grafting. Following induction of anesthesia, before and after volume replacement (6% hydroxyethyl starch solution, 10 mL/kg ideal body weight), hemodynamic measurements of stroke volume index (SVI), SVV, PPV, global end-diastolic volume index (GEDVI), central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) were obtained. A significant correlation with changes of SVI was observed for SVV ($r = 0.606$, $p < 0.001$) and PPV ($r = 0.612$, $p < 0.001$) only. SVV and PPV were closely related ($r = 0.861$, $p < 0.001$).They concluded that In contrast to standard preload indexes, SVV and PPV, comparably, showed a good performance in predicting fluid responsiveness in patients before off-pump coronary artery bypass grafting.

Heenan et al (critical care 2006)[17] evaluated the ability of different static and dynamic measurements of preload to predict fluid responsiveness in patients with spontaneous respiratory movements in 21 critically ill patients with spontaneous breathing movements receiving

mechanical ventilation with pressure support mode (n = 9) or breathing through a face mask (n = 12), and who required a fluid challenge. Complete hemodynamic measurements, including pulmonary artery occluded pressure (PAOP), right atrial pressure (RAP), pulse pressure variation (ΔPP) and inspiratory variation in RAP were obtained before and after fluid challenge. Fluid challenge consisted of boluses of either crystalloid or colloid until cardiac output reached a plateau. Receiver operating characteristics (ROC) curve analysis was used to evaluate the predictive value of the indices to the response to fluids, as defined by an increase in cardiac index of 15% or more. There were no significant differences in ΔPP, PAOP, RAP and inspiratory variation in RAP between fluid responders and non-responders. Fluid responsiveness was predicted better with static indices (ROC curve area ± SD: 0.73 ± 0.13 for PAOP, $p < 0.05$ vs ΔPP and 0.69 ± 0.12 for RAP, $p = 0.054$ compared with ΔPP) than with dynamic indices of preload (0.40 ± 0.13 for ΔPP and 0.53 ± 0.13 for inspiratory changes in RAP, p not significant compared with ΔPP).The authors concluded that in patients with spontaneous respiratory movements, ΔPP and inspiratory changes in RAP failed to predict the response to volume expansion.

Kubitz et al (BJA 2007)[21] compared left ventricular SVV derived by pulse contour analysis with SVV measured using an ultrasonic flow probe and investigated the influence of cardiac afterload on left ventricular SVV in 13 anaesthetized, mechanically ventilated pigs . After obtaining baseline measurements, cardiac afterload was increased using phenylephrine and decreased using adenosine (both continuously administered). Measurements were performed with a constant tidal volume (12 ml kg-1) without PEEP. Neither increasing mean arterial pressure (MAP) [from 59 (7) to 116 (19)] nor decreasing MAP [from 63 (7) to 39 (4)] affected CO, SV, and SVV (both methods). The authors concluded that left ventricular SVV is not affected by changes in cardiac afterload. There is a good agreement of pulse contour with flow derived SVV.

Reuter et al (Intensive care 2003)[44] investigated the influence of the depth of tidal volume (V(t)) on SVV both during the state of fluid responsiveness and after fluid loading in mechanically ventilated patients in 20 hemodynamically stable patients immediately after cardiac surgery.Stepwise fluid loading using colloids until stroke volume index (SVI) did not increase by more than 10%. Before and after fluid loading V(t) was varied (5, 10, and 15 ml/kg body weight) in random order.Pulse contour SVV was measured before and after volume loading at the

respective V(t) values. Thirteen patients responded to fluid loading with an increase in SVI greater than 10%, which confirmed volume responsiveness at baseline measurements. These were included in further analysis. During volume responsiveness SVV at V(t) of 5 ml/kg (7+/-0.7%) and SVV at V(t) of 15 ml/kg (21+/-2.5%) differed significantly from that at V(t) of 10 ml/kg (15+/-2.1%). SVV was correlated significantly with the magnitude of V(t). After volume resuscitation SVV at the respective V(t) was significantly reduced; further, SVV at V(t) of 5 ml/kg(-1) (5.3+/-0.6%) and 15 ml/kg (16.2+/-2.0%) differed significantly from that at V(t) of 10 ml/kg (10.2+/-1.0%). SVV and depth of V(t) were significantly related.The authors concluded that in addition to intravascular volume status SVV is affected by the depth of tidal volume under mechanical ventilation. This influence must be regarded when using SVV for functional preload monitoring.

Marik PE, Baram M, Vahid B. Et al(Chest 2008)[26] did a systematic review of the literature to determine the following: (1) the relationship between CVP and blood volume, (2) the ability of CVP to predict fluid responsiveness, and (3) the ability of the change in CVP (DeltaCVP) to predict fluid responsiveness. 24 studies were taken into account which included 803 patients; 5 studies compared CVP with measured circulating blood volume, while 19 studies determined the relationship between CVP/DeltaCVP and change in cardiac performance

following a fluid challenge. The pooled correlation coefficient between CVP and measured blood volume was 0.16 (95% confidence interval [CI], 0.03 to 0.28). Overall, 56+/-16% of the patients included in this review responded to a fluid challenge. The pooled correlation coefficient between baseline CVP and change in stroke index/cardiac index was 0.18 (95% CI, 0.08 to 0.28). The pooled area under the ROC curve was 0.56 (95% CI, 0.51 to 0.61). The pooled correlation between Delta CVP and change in stroke index/cardiac index was 0.11 (95% CI, 0.015 to 0.21). Baseline CVP was 8.7+/-2.32 mm Hg [mean+/-SD] in the responders as compared to 9.7+/-2.2 mm Hg in non responders (not significant).This systematic review demonstrated a very poor relationship between CVP and blood volume as well as the inability of CVP/Delta CVP to predict the hemodynamic response to a fluid challenge. The authors concluded that CVP should not be used to make clinical decisions regarding fluid management.

Frederic Michard,, Jean Louis Teboul MD et al(Critical care review 2002)[33] did a literature review and analysis of 12 studies of fluid responsiveness in ICU patients. 334 pts, 406 fluid challenges were included of which 55% patients were in sepsis, 84% on mechanical ventilation. RAP (CVP) was measured. No baseline difference in responders vs. non-responders in 3/5 studies.

METHODS

STUDY DESIGN

This study was a prospective observational study conducted in Government Stanley Medical College and Hospital, Chennai.

STUDY SETTING AND POPULATION:

The Institutional Ethical committee approval was obtained before commencement of the study. Written informed consent was obtained from all the patients. Twenty five adult patients of ASA Physical status 1& 2 of either sex undergoing elective abdominal surgical procedures under general anaesthesia were enrolled in the study.

The study was conducted at the Surgical gastroenterology theatre complex, Stanley Medical College and Hospital, Chennai. The study was conducted from May 2011 to August 2011.All major abdominal surgeries within this period who fit into the inclusion criteria were included in the study.

PATIENT SELECTION

Inclusion criteria:

Elective major abdominal surgery (intestine resection, gastric resection,

Whipple procedure, frey procedure) .

Both genders

Age 18-60 YRS

ASA PS I/II

Exclusion criteria:

Patients under 18 years.

Patient > 60 yrs

ASA PS III/IV

Patients with severe aortic regurgitation,

Patients with renal impairment

Permanent cardiac arrhythmias,

Intra-aortic balloon pump

Patients undergoing emergency surgery

were excluded from the study.

Study Materials:

The materials need for the study included

Intravenous Cannula

Drugs for general anesthesia

Inj. Fentanyl

Inj. Propofol

Inj. Atracurium

Appropriate size endotracheal tubes and laryngoscopes

Standard Monitors – pulse oximeter, ECG, NIBP,ETCO2

All emergency drugs

Anesthesia Ventilator

Arterial Catheter 20 G

Central venous catheter 7 Fr

Vigileo Flotrac monitor with transducer.

Study Methods:

After obtaining ethical committee clearance Twenty five patients of similar age group, weight and equal sex distribution were included in the study. Informed written consent was obtained. Detailed history of past medical/surgical were obtained.

Anesthetic technique:

Standard monitors: electrocardiogram, pulse oximetry, Non invasive blood pressure, Temperature probe were connected to the patient. Baseline demographic parameters, blood pressure, and heart and respiratory rates were recorded. Peripheral venous access obtained with 18G venflon. Epidural catheter was inserted between the Thoracic D10/11 vertebral interspaces and after performing a test for correct epidural placement, a dose of morphine 4mg in 10 ml saline solution[49] was administered.

The left wrist was immobilized with dorsiflexion with a tape across the thumb.20 Gauge needle over catheter was used to cannulate left radial artery. The artery was palpated 2-3 cm along its course, the 20G needle was inserted at an angle of 30 degrees and advanced toward the pulsation in rapid short 1 mm increments. When the artery was entered, catheter unit advanced several millimetres to transfix the artery, needle completely removed, catheter is backed until good flow returns, then advanced directly into the artery. Arterial blood flow from the catheter was confirmed and the transducer tubing was attached. Once arterial waveform was observed sterile dressing applied over it. Blood pressure was recorded after connecting to transducer zeroed at mid-axillary level.

Optimal pressure signal damping was assessed using flush test before the first measurements. Vigileo/FloTrac device [24](Edwards Lifesciences, Irvine, CA, USA) with software version 1.10 was used for measuring Stroke volume variation(SVV) and other hemodynamic variables like CI, Stroke volume index SVI.

The FloTrac™ transducer was fitted in the regular pole mounted holder with stopcock above transducer.

Then the Vigileo™ monitor was switched on. The patient's height, Weight, gender were entered. The transducer was levelled and zeroed. Automated calculation of SVV was displayed in real-time by the Vigileo monitor (software version 1.10). SVV was assessed using a proprietary algorithm discussed elsewhere. The system showed a continuous monitoring of arterial pressure, CO, SV, and SVV by pulse contour analysis from the arterial pressure wave. This system required no calibration.

Anesthesia was then induced using propofol 2 mg/kg in combination with fentanyl 2 ug/kg .Tracheal intubation done with neuromuscular relaxation atracurium 0.5mg/kg and confirmed with end tidal CO2. Anesthesia was maintained with volatile anesthetics (sevoflurane) in N_2O and O_2 mixture .

A 7 Fr central venous catheter[35] was inserted via right internal jugular vein .The neck was turned to the opposite side & 15-20 degree trendelenberg position was given. A rolled up towel was placed between the scapulae to extend the head & accentuate the landmarks. The neck was prepared with povidone iodine .The triangle formed by the two heads of sternocleidomastoid & clavicle was identified. The carotid artery at the medial end of this triangle was palpated. Near the apex of this triangle, skin puncture was made at 30degree directed towards the ipsilateral nipple.

With constant aspiration, the needle was slowly advanced till blood was aspirated. The internal jugular vein was cannulated by modified Seldinger's technique. The distal port was connected to a transducer and central venous pressure was recorded. The hub of the cannula was anchored with two sutures. Central venous pressure (CVP) was continuously measured by using a transducer calibrated to the mid axillary level. Sufficient analgesia was provided using a continuous infusion of Inj fentanyl 0.5 mcg/kg/hr.

All patients were mechanically ventilated with tidal volume 10ml/kg and positive end-expiratory pressure (PEEP) 3, respiratory rate 12 to maintain normocapnia.

Protocol:

After induction all patients were maintained on Ringer lactate based on 4-2-1 formula[35]. Half an hour after induction a first volume loading step was performed with 100 mL of colloid solution (6% hydroxyethylstarch) for 2 min in the peripheral IV line. Hemodynamic variables were recorded prior to the administration of the volume loading step. The hemodynamic variables were recorded again 1 min after the end of the infusion. The volume loading step (VLS) were termed

- **Responsive VLS** when there was an increase in stroke volume SV by at least 5%
- **Nonresponsive VLS** when there was no change or the increase in stroke volume SV was less than 5%.

Volume loading steps were conducted every 30 minutes after the first VLS. Each patient underwent multiple volume loading steps every thirty minutes until three responsive and three non responsive volume loading steps were obtained. Six volume loading steps three responsive and three non responsive were obtained from each patient and were analysed. In each patient, When a volume loading step was responsive another VLSs were performed until a nonresponsive VLS was reached.

Hemodynamic monitoring:

Mean blood pressure, Systolic blood pressure(SBP), Diastolic blood pressure Heart rate(HR),Stroke volume(SV), and Stroke volume variation(SVV) were continuously measured before the volume loading step and one minute after the completion of volume loading step.

STATISTICAL ANALYSIS

Twenty five patients of either sex belonging to ASA PS 1 & 2, undergoing elective abdominal procedures under general anaesthesia were studied. Each patient underwent six volume loading steps. A total of 150 volume loading steps were performed.

- All hemodynamic variables were analyzed as continuous variables and expressed as the mean ± SD.
- To determine whether hemodynamic variables changed in relation to volume loading, differences between values before and after each VLS were compared between responsive and nonresponsive VLSs by using a Paired sample t-test.
- The correlation between changes in SV and changes in hemodynamic variables was assessed by using Pearson's correlation test.
- Receptor operation characteristic curves[29] were drawn for each hemodynamic variables and the area under the curve was obtained.

All data analysed using SPSS 16.0 version (SPSS Inc., Chicago, IL)

OBSERVATION AND RESULTS

GENDER: Table 1

Gender	N	Percentage
Male	12	48
Female	13	52
Total	**25**	**100**

Table-2 Age

	Mean	Sd	t-value	p-value
Male	39.67	12.06	0.21	0.84
Female	35.15	10.78		Not Significant
Total	37.3	11.47		

12 Male patient and 13 female patients with a mean age of 37.3 +/- 11.47 years participated in this study.

AGE DISTRIBUTION: Table 3

Age	Male		Female		Total	
(in Years)	**N**	**%**	**N**	**%**	**N**	**%**
20 – 30	3	25.00	5	38.46	8	32.00
30 – 40	4	33.33	5	38.46	9	36.00
40 – 50	3	25.00	2	15.38	5	20.00
50 – 60	2	16.67	1	7.69	3	12.00
Total	12	100.00	13	100	25	100.00

Chi squre =2.99 df=3 p=0.39

These twenty five patients were evenly distributed between the various age groups between 20-60 years.

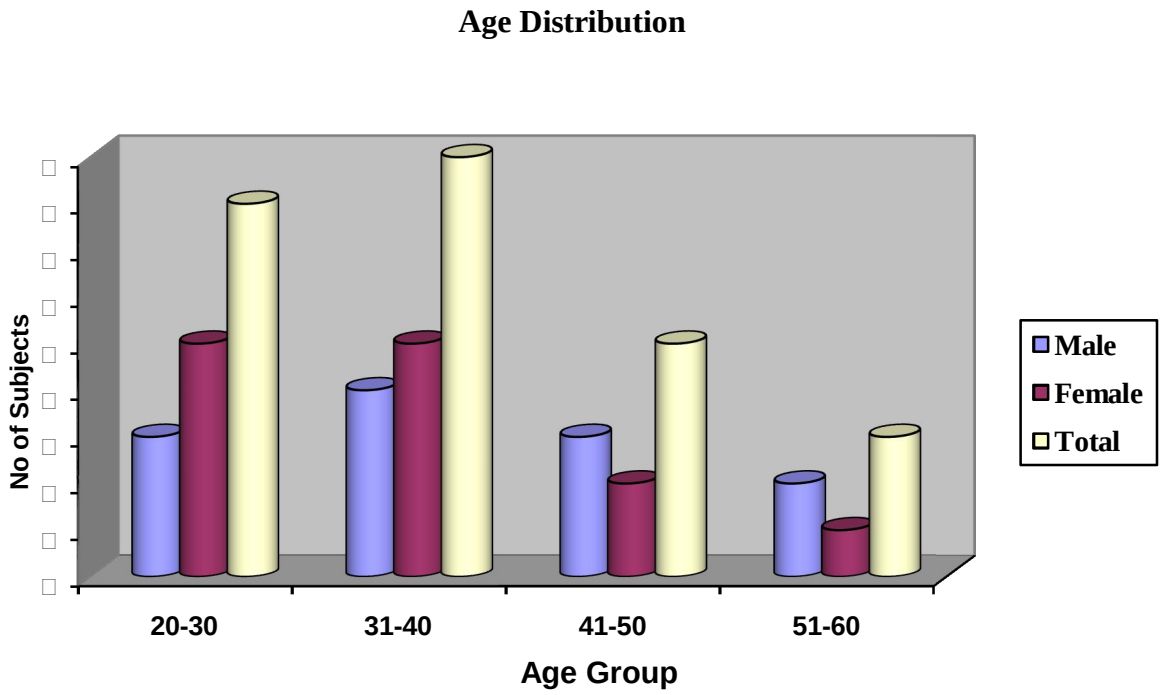


Fig 11: AGE DISTRIBUTION

Table-4:

	Mean	Sd
BSA	1.57	0.06
Height in cm	158.96	3.93
Weight in kg	55.36	3.41

Table 5 :Type of Surgery:

SURGERY	NUMBER
Frey procedure	**12**
Whipple procedure	**7**
Hepato jejunostomy	**6**

Hemodynamic Variables Before Fluid Loading

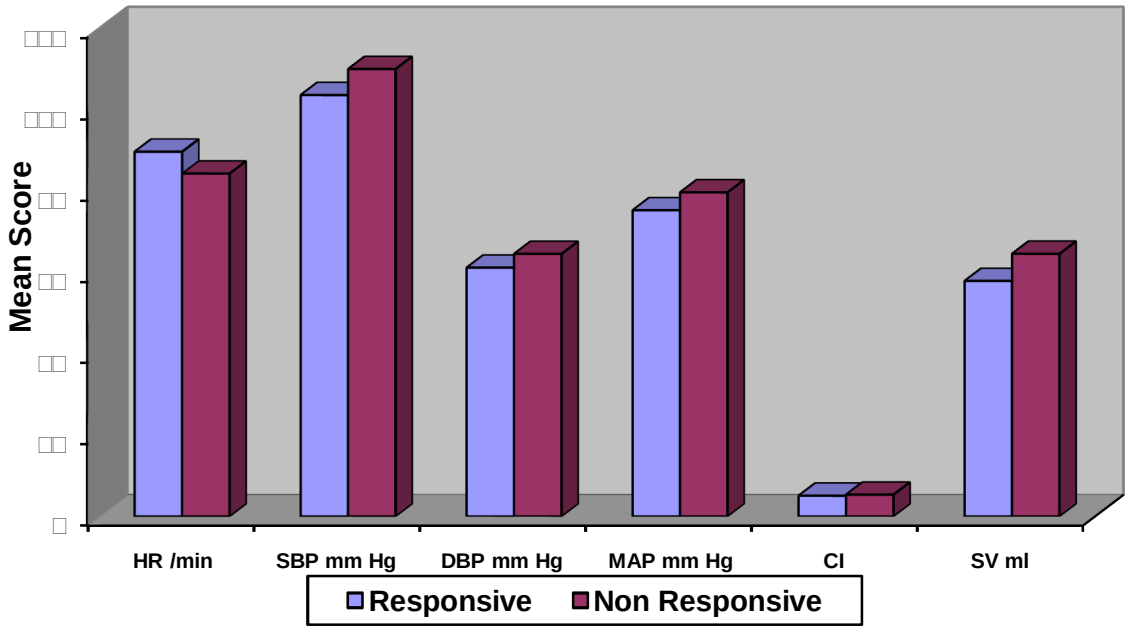


Table-6: Hemodynamic Variables before Fluid Loading

Variables	Responsive		Non Responsive		t-value	P-value
	Mean	Sd	Mean	Sd		
HR	89.67	15.21	84.29	13.85	2.26	0.03
Systolic	103.59	7.17	109.99	6.26	5.82	0.001*

Diastolic	61.16	5.90	64.55	5.10	3.76	0.001*
MAP	75.28	5.40	79.67	4.41	5.45	0.001*
CI	5.10	0.62	5.36	0.58	2.71	0.01*
SV	57.89	8.58	64.57	7.67	5.03	0.001*

*p value significant.

Before fluid loading SBP, MAP, DBP were significantly lower in responsive patients. Heart rate showed no significant difference in responsive and non responsive patients.

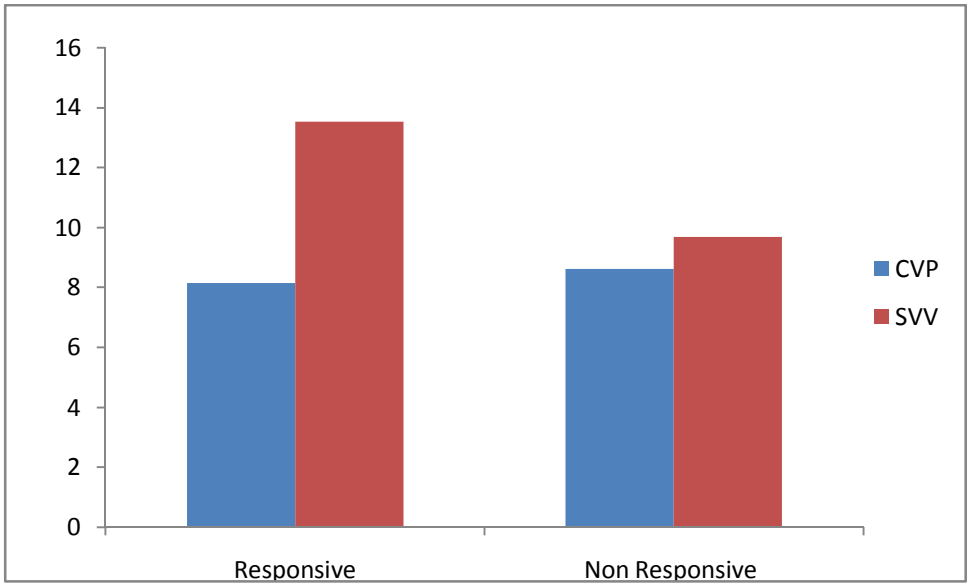


Fig 12: SVV VS CVP before fluid loading

Table **7: SVV & CVP before fluid loading:**

	Responsive		Non Responsive			
	Mean	SD	Mean	SD	T value	P value
CVP	8.41	0.887	8.59	0.96	1.158	0.249
SVV	13.53	2.49	9.67	1.34	11.85	0.001*

*P value significant

BEFORE FLUID LOADING CVP vs SVV

In responders SVV were significantly higher.

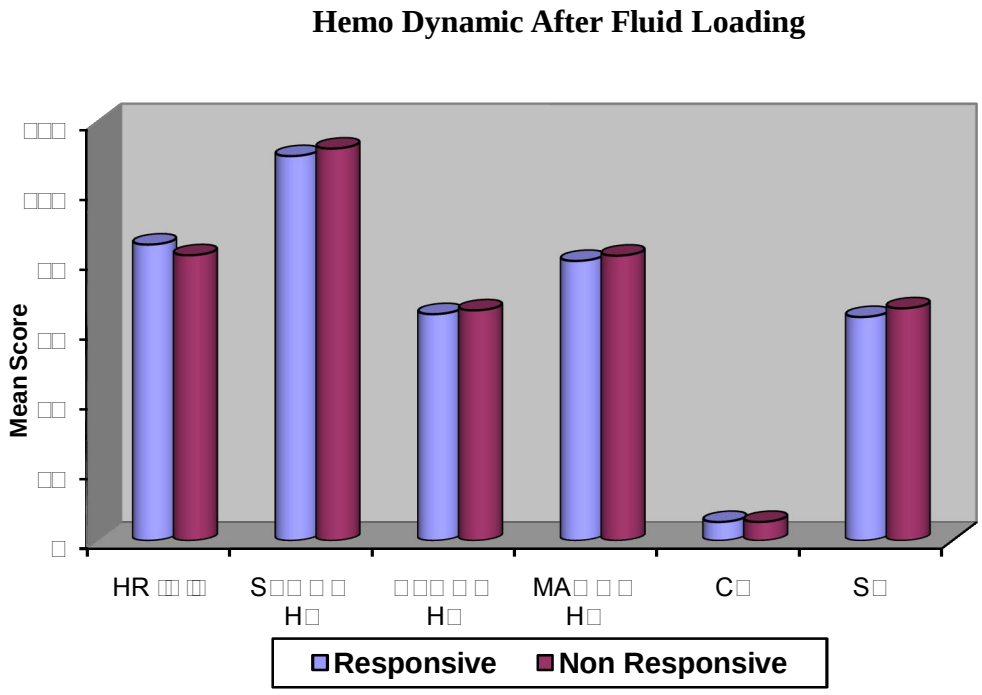


Fig 13: Hemodynamic variables after fluid loading.

Table-8: Hemodynamic Variables after Fluid Loading

Variables	Responsive		Non Responsive		t-value	P-value
	Mean	Sd	Mean	Sd		
HR	84.89	13.30	81.83	12.84	1.44	0.153
Systolic	110.25	6.26	112.40	5.92	2.16	0.03
Diastolic	64.95	4.80	66.03	4.63	1.40	0.163
MAP	80.20	4.41	81.71	4.06	2.18	0.03
CI	5.37	0.56	5.38	0.56	0.13	0.90
SV	64.12	8.06	66.61	7.66	1.94	0.05

No statistical difference was observed after fluid loading with respect to HR, MAP, systolic and diastolic blood pressure .

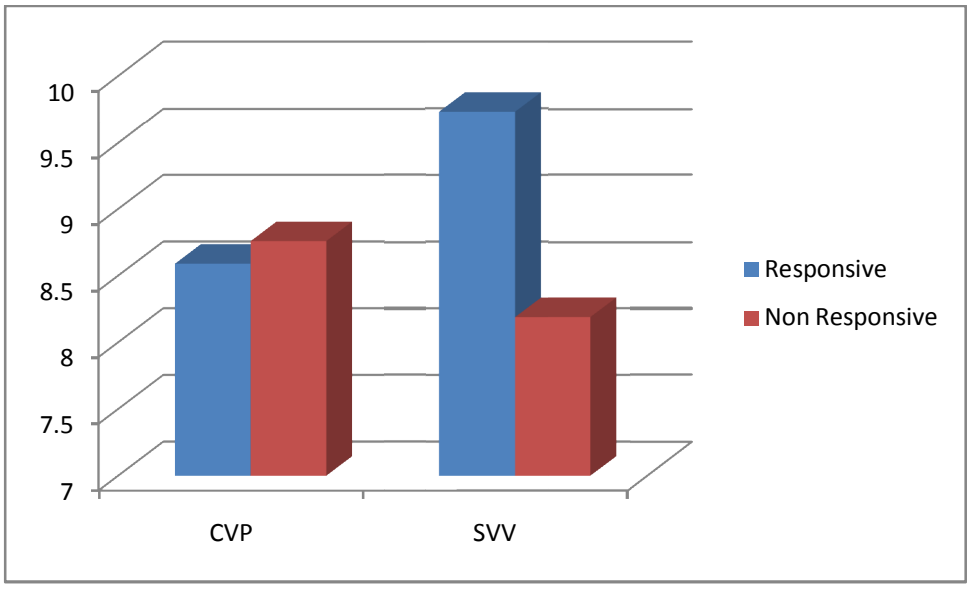


Fig 14: SVV Vs CVP after fluid loading

Table 9: SVV Vs CVP after fluid loading

	Responsive		Non Responsive			
	Mean	SD	Mean	SD	T value	P value
CVP	8.59	0.93	8.77	0.86	1.27	0.205
SVV	9.73	1.39	8.19	1.04	7.73	0.001*

*P value significant

Hemodynamic variables after fluid loading ,In Non responders SVV were significantly lower .

No statistical difference was observed after fluid loading with respect to CVP.

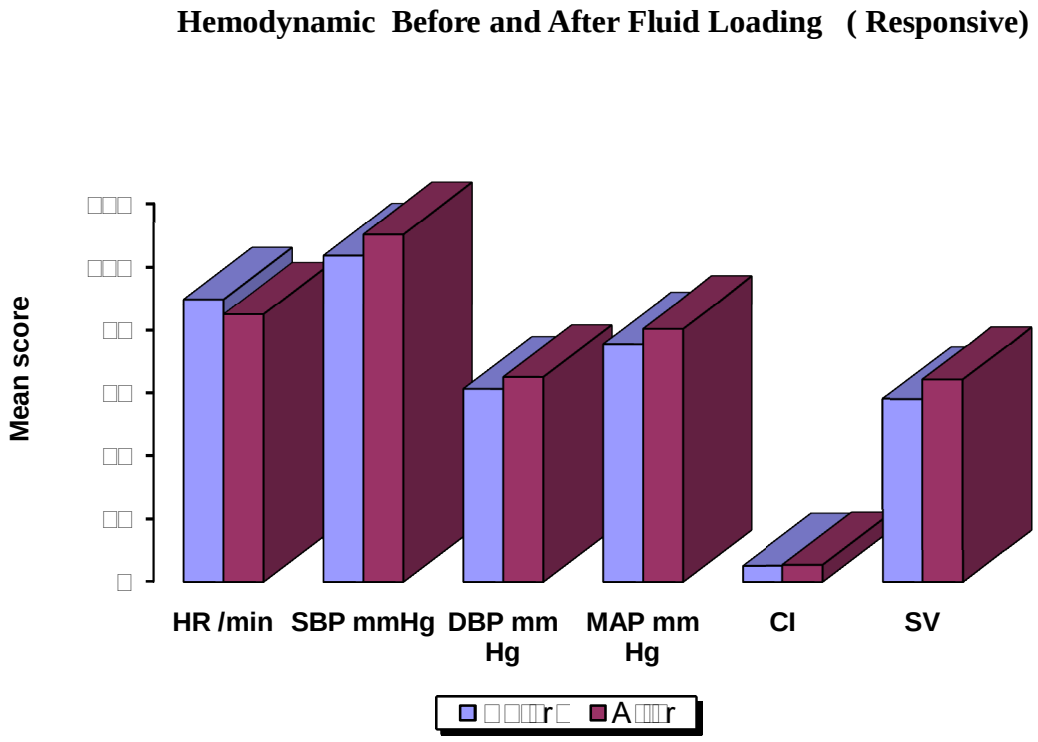


Fig 15: Hemodynamic Variables Before and After fluid Loading (Responders)

Table-10 Hemodynamic Variables Before and After fluid Loading (Responders)

Variables	Before		After		t-value	P-value
	Mean	Sd	Mean	Sd	(Paired)	
HR	89.67	15.21	84.89	13.30	11.66	0.09
Systolic	103.59	7.17	110.25	6.26	13.44	0.001*
Diastolic	61.16	5.90	64.95	4.80	12.29	0.001*
MAP	75.28	5.40	80.20	4.41	14.52	0.001*
CI	5.10	0.62	5.37	0.56	9.59	0.001*
SV	57.89	8.58	64.12	8.06	19.02	0.001*

*P value significant

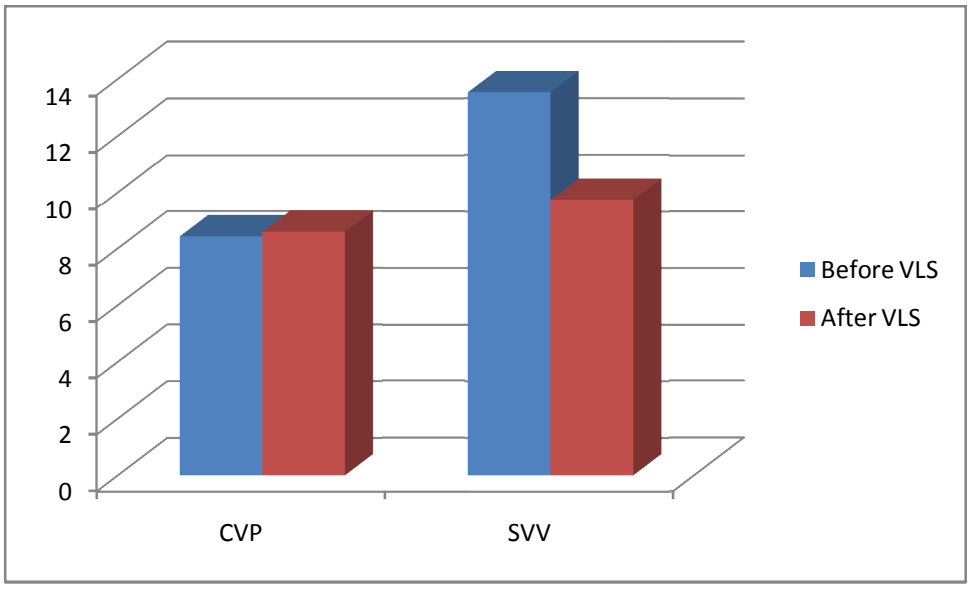


Fig 16: RESPONSIVE PATIENTS BEFORE AND AFTER FLUID LOADING SVV Vs CVP

Table 11: RESPONSIVE PATIENTS BEFORE AND AFTER FLUID LOADING SVV Vs CVP:

	Before fluid loading		After fluid loading			
	Mean	SD	Mean	SD	T value	P value
CVP	8.41	0.88	8.59	.93	1.22	0.23
SVV	13.53	2.49	9.73	1.39	19.00	0.001*

*P value significant.

In responders the Change in SVV, Systolic, diastolic blood pressure, MAP, were statistically significant. Change in CVP, HR were not statistically significant.

Table-12: The correlation between Hemodynamic variables to Change in SV :

Variables	**Pearson's Correlations (r)**	**P-Value**	**Significant**
Change in CVP	0.066	P = 0.422	NS
Change in SVV	-0.584	P < 0.001	Significant

Significant correlation was found between the change in SV and the changes in SVV. No significant correlation was found between the changes in SV and the values of the CVP .

To assess the ability of different hemodynamic variables to discriminate between positive (>5% increase in SV) and negative (<5% increase in SV) response to fluid challenge, receiver operating characteristic (ROC) curves were generated for HR, SBP,MAP,DBP,

CVP, and SVV, varying the discriminating threshold of each variable. The area under the ROC curve for each variable was calculated and compared. Values for each area can be between 0 and 1. A value of 0.5 indicates that the screening measure is no better than chance, whereas a value of 1 implies perfect performance.

In our study, the area under the ROC curve represented the probability that a random pair of responsive and nonresponsive VLSs would be correctly ranked the hemodynamic variable

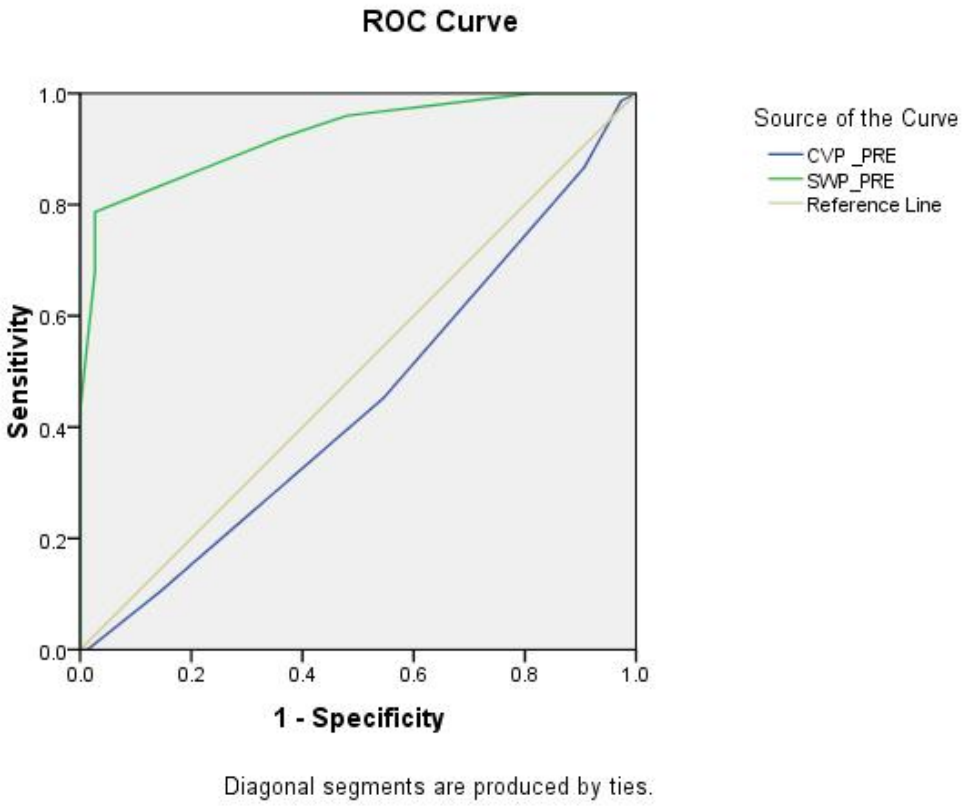


Fig 17: ROC curve for SVV Vs CVP:

SVV AUC 0.925 95%CI 0.884-0.967 p=0.0001*

CVP AUC 0.424 95%CI 0.292-0.471 p=0.107

Area under the curve was more (SVV AUC=0.925) and statistically significant for stroke volume variation. Area under the curve for CVP was < 0.5 (CVP AUC=0.424).

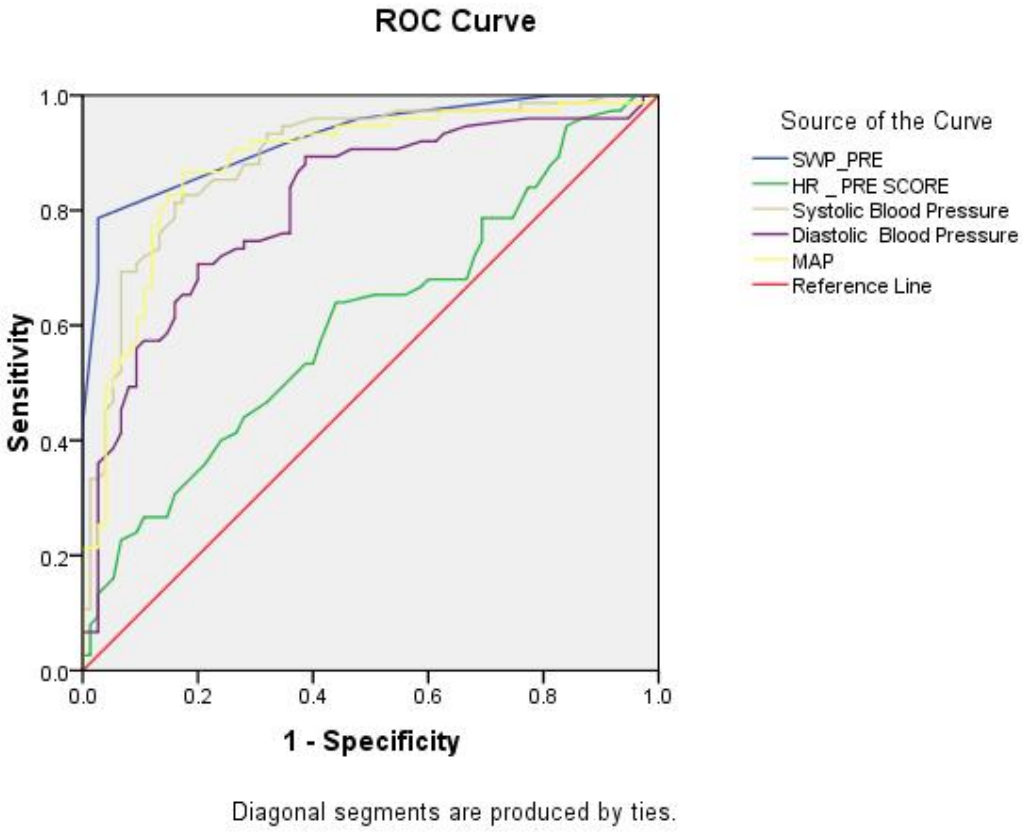


Fig 18: ROC Curve for SVV, MAP, Systolic, diastolic blood pressure, HR.

Systolic blood pressure AUC 0 .891 95% CI 0.838-0.944 p=0.0001*

Diastolic blood pressure AUC 0.811 95%CI 0.741-0.881 p=0.0001*

MAP AUC 0.883 95%CI 0.827-0.939 p=0.0001*

HR AUC 0.606 95% CI 0.515-0.696 p=0.025

Based on the area of curve fluid responsiveness the order of sensitivity for fluid responsiveness was found to be SVV> SBP >MAP > DBP > HR >CVP in our study.

RESULTS/DISCUSSIONS

Our study which had Twenty five patients which included 12 male patients, 13 female patients showed that the stroke volume variation as a reliable predictor of fluid responsiveness in comparison with the central venous pressure in elective major abdominal procedures.

Twenty five patients 12 male and 13 female aged 37.3+/- 11.47 yrs participated in this study. Twelve patients of ASA PS I, thirteen patients of ASA PS II with mean height of 158.96 +/- 3.93 cms mean weight in kilograms of 55.36+/-3.41 kg with body surface area of 1.57 +/- 0.06in Sq.meters participated in this study. The patients were distributed evenly through various age groups.

In patients undergoing major abdominal surgery[37], preoperative fasting, Hyperosmolar enema, induction of general anesthesia, epidural analgesia and intraoperative bleeding decrease intravascular volume, blood pressure, as a result leads to compromise perfusion of organs.

Assessment of circulating blood volume[10] is necessary for perioperative fluid management. Hence patients who underwent elective abdominal procedures who fulfilled our inclusion criteria during our study period were included. So a total of twenty five patients participated in the study of which seven patients underwent whipple's procedure, Six

patients underwent Hepatojejunostomy/CBD exploration, twelve patients underwent frey's procedure.

Patients of less than 18 years and more than sixty years were not included in the study to avoid the influence of extremes of age. Patients who had dysrhythmia were also excluded because if filling of the ventricles is changing on a beat-to-beat interval because of a significant dysrhythmia, there is significant variation in stroke volume simply related to the variability in filling time caused by the irregular rhythm that will not reflect volume responsiveness. Simply, there can be tremendous stroke volume and pulse pressure variability with a significant dysrythmia that is related to the rhythm problem itself and not volume status. In these instances, stroke volume variation or pulse pressure variation tells us nothing about volume responsiveness or the patient's position on the Frank-Starling curve. This is also the reason why stroke volume variation is not effective in case of spontaneous ventilation due to non uniformity of each breath.

All these patients were mechanically ventilated performed in a volume-controlled mode. Fonseca et al[14] who compared different modes of ventilation in graded hypovolemia concluded in his study that under normovolaemia and moderate haemorrhage, dynamic parameters were not influenced by either ventilatory modalities. However, in the second

stage of haemorrhage (30%), volume-controlled ventilation presented higher values of systolic pressure variation and pulse pressure variation when compared with those submitted to pressure-controlled ventilation. Hence volume controlled mode was chosen.

In addition to intravascular volume status, SVV is affected by the depth of airway pressure, respiratory rate. De backer et al[12] concluded that respiratory variations in stroke volume and its derivates are affected by respiratory rate. The study suggests that right and left indices of ventricular preload variation are dissociated at higher respiratory rates. **At high respiratory rates, the ability to predict the response to fluids of stroke volume variations and its derivate may be limited.**

SVV depends on a positive-pressure breath and therefore could be influenced by large tidal volumes[11], reduced chest wall compliance, and air trapping may cause exaggerated SVV values. Reuter et al.[44] investigated the influence of the depth of tidal volume (Vt) on SVV both during the state of fluid responsiveness and after fluid loading in mechanically ventilated patients and concluded that during volume responsiveness SVV at Vt of 5 ml/kg(7+/-0.7%) and SVV at Vt of 15 ml/kg (21+/-2.5%) differed significantly from that at Vt of 10 ml/kg (15+/-2.1%). **SVV was correlated significantly with the magnitude of tidal volume** . As Szold et al demonstrated that increased tidal volumes

lead to progressively larger decreases in left ventricle stroke volume LVSV and increase in SVV.

However, Feissel et al [15] found that analysis of respiratory changes in aortic blood velocity , Left ventricular stroke volume is an accurate method for predicting the hemodynamic effects of volume expansion in septic shock patients receiving mechanical ventilation using tidal volumes of 8-10ml/kg.

Renner et al [42] studied the effects of different levels of PEEP on SVV, pulse pressure variation. At PEEP 5 cmH2O, SVV, PPV significantly correlated with volume induced percentage change in SV, whereas at PEEP 10 cmH(2)O, this correlation was abolished for PPV and to a lesser extent for SVV. **Thus, tidal volume of 10ml/kg was decided with a PEEP of 3 cm H_2O, and respiratory rate of 12.** These parameters remained stable during the procedure. During the study period, no significant changes in peak or plateau inspiratory pressure were identified.

Various studies evaluating [1,3,18] dynamic indices in their studies have used different fluid and volume with regard to the fluid challenge. Berkenstadt et al[3] had used 100ml of colloid over 2 minutes with a response of an increase in stroke volume by 5%. Hofer et al in his study

had used 500 ml of crystalloid solution with an arbitrary increse in cardiac output by more than 15 % for responders. The crystalloid–colloid controversy includes the role of colloid osmotic pressure in plasma in retaining fluids intravascularly and in the speed and extent to which colloids restore plasma volume and blood flow as opposed to crystalloids, which dilute plasma proteins, lower Colloid oncotic pressure and rapidly leak into the interstitium . When using crystalloids, two to four times more fluid may be required to restore and maintain intravascular fluid volume compared with colloids. Hence it was chosen to use colloid for the fluid challenge . 100 ml of colloid over 2 minutes was chosen as the volume for fluid loading with an increase in stroke volume by 5 % as the criteria for patients who are fluid responsive.

Vigileo flotrac monitor[24] (Edwards Lifesciences, Irvine, CA, USA) with software version 1.10 was used for measuring Stroke volume variation(SVV) and other hemodynamic variables like Cardiac output, Stroke volume index SV. The Vigileo monitor offers uncalibrated CO measurement by arterial waveform analysis. Sanders[46] et al conducted a validation study in cardiac patients compared CO measurements derived from radial artery waveform analysis with those derived from the ascending aorta. CO measurements from the radial artery versus the

ascending aorta showed a significant correlation before and after cardiopulmonary bypass (CPB).

Hofer[19] et al compare the 2 proprietary APCO algorithms as Flotrac vigileo /PICCO alternatives to pulmonary artery catheter thermodilution in orthotopic liver transplantation (OLT). Kubitz et al [21]compared left ventricular SVV derived by pulse contour analysis to an experimental *gold standard* method (aortic flow probe) in anesthetized pigs; also investigated whether left ventricular SVV was affected by induced changes in cardiac afterload . The authors concluded that left ventricular SVV was not affected by changes in cardiac afterload . There was good agreement between pulse contour derived SVV and a *gold standard* comparator, whereas SV was found to be overestimated by pulse contour analysis.

Biais et al[4] SVV derived from a peripheral artery by the Vigileo/FloTrac system and SVV derived close to the heart by aortic Doppler measurements showed a similar performance in terms of identifying fluid responsiveness in patients undergoing Liver transplantation.

Each patient underwent six volume loading step. A total of 150 volume loading steps (VLS) were performed. In 75 VLS, an increase in stroke volume SV of more than 5% occurred and they were termed as responsive while in 75 VLS stroke volume increased by less than 5% and were termed as non responsive. In all 75 responsive VLS unresponsiveness was reached after the second loading. The data from the second loading were not included in the analysis.

Responders and non responders differed significantly in their pre VLS values .In responders before fluid loading, SVV were significantly higher and CVP were significantly lower as in conjunction with the study by biasis[4] et al. SVV in responders was 13.53 +/- 2.49 % before fluid loading. According to our study **When SVV was elevated (≥13%), patients were on the preload dependent part of the frank starling curve and they responded to volume loading.** In non responders prior to fluid loading SVV was 9.67 +/- 1.34 which was significantly lower. When SVV was less than 10% the patients were on the independent part of the frank starling curve hence they did not respond to the volume loading with an increase in stroke volume.

In comparing Responsive VLSs, it was found that significant SVV changes were seen before and after fluid loading. SVV changed from

13.5% to 9.73 %. However the change of central venous pressure was not significant.These findings were corroborative with the study conducted by Berkenstadt et al[3].

Statistically significant correlations were found between the change in SV and the values of SVV(r=-0.584) before fluid loading. No correlation was found between the changes in SV and the values of the CVP(r=-0.066). Berkenstadt et al also had come to a similar observation in his study.Hofer et al found no significant correlations of CVP with ΔSV in a study comparing SVV to pulmonary artery catheterization by thermodilution in mechanically ventilated patients . The study concluded that CVP performed poorly as a measure of preload responsiveness

The failure of CVP[38] in predicting fluid responsiveness is in accordance with increasing evidence that static preload indicators are not suited for functional haemodynamic monitoring. In contrast, a growing number of clinical studies have clearly demonstrated the ability of dynamic preload indicators (including SVV) [7,18,48]to accurately predict the response of an individual patient to a volume challenge.

The overall performance of preload variables in predicting the responsiveness of the SV to VLS was evaluated by constructing ROC curves. **Receptor operation characteristics curve generated in our**

study showed the area under the curve for SVV (0.891), CVP (0.643), MAP (0.783), SBP (0.791), DBP (0.781). The area for SVV was statistically more than those for CVP, HR, and SBP as concluded by Berkenstadt et al.[3] whose ROC area under the curve for svv was 0.89. Hofer et al in his study obtained a ROC of 0.82 for SVV. Based on the area of curve **the order of sensitivity for predicting fluid responsiveness** as determined by a hemodynamic variable was found to be **SVV> SBP >MAP > DBP > HR >CVP** in our study with CVP having an area of less than 0.5

The optimal threshold values given by ROC analysis in our study was 10.5 % for SVV with a sensitivity of 92% and a specificity of 64%. Cannessoon et al[7] concluded that a threshold SVV value of 10% allowed discrimination of responders to VE with a sensitivity of 82% and a specificity of 88%. Hofer and colleagues[18] reported that an SVV threshold value of ≥12% is able to predict an SVI increase ≥25% with a sensitivity of 74% and a specificity of 71% achieving an area under the ROC curve of 0.808 in patients undergoing off-pump cardiac surgery. Berkenstadt[3] and colleagues calculated a threshold value for SVV above 9.5% to induce a ≥5% increase in SVI after administering a stepwise fluid bolus of hydroxyethyl starch 130/0.4 6% (100 ml) in patients undergoing brain surgery. Recently, Hofer and colleagues reported an

SVV threshold value of 9.6% (sensitivity 91%, specificity 83%, area under the ROC curve 0.824) for prediction of fluid responsiveness (SVI increase >25 %) in patients before elective cardiac surgery using the FloTrac™/Vigileo™ system.

The uncertainty that characterizes current decision-making about fluid administration is because of the lack of physiological variables that will successfully predict the response to fluid loading. Clinical examination, arterial blood pressure, heart rate, and even central venous and pulmonary artery occlusion pressure, have repeatedly been shown to be poor predictors of fluid responsiveness, and to be unable to differentiate between patients who respond to intravascular volume loading (responders) and patients who do not (non responders). Even more accurate measures of preload, such as the global end-diastolic volume, the left ventricular (LV) end-diastolic area, and the right ventricular end-diastolic volume, are mediocre predictors of fluid responsiveness, since the relationship of any static “preload” variable to the response of the CO to fluid loading depends on the elusive slope of the LV function curve.

A dynamic approach to assess fluid responsiveness is offered by measuring the effect of the decrease in venous return on the cardiac output during a mechanical positive-pressure breath. During the last 20 yr, an increasing number of publications have described the usefulness of

variables such as the systolic pressure variation (SPV), stroke volume variation (SVV), and a variety of other variables, which reflect the hemodynamic changes that occur during mechanical ventilation. For many of these variables, this “respiratory variation” has been shown to be a better predictor of fluid responsiveness than commonly measured static preload variables. However, the penetration of functional hemodynamic variables into mainstream clinical practice has been exceedingly slow. Currently the change in CVP following a fluid challenge is used to guide fluid management decisions. Since CVP plays such a central role in the fluid management strategy of hospitalized patients and it has been shown to be a poor predictor for fluid responsiveness dynamic indices like stroke volume variation SVV should be incorporated for effective intraoperative fluid management.

The limitations of the study was although the ability of SVV to accurately predict fluid responsiveness was demonstrated, that other preload variables such as SPV, PAOP, or LV end diastolic area, were not measured simultaneously with the SVV. Other limitations of the study are that the study protocol was performed by the anesthesiologist treating the patient without any blinding, the fact that multiple measurements were performed in the same patients, and the need for an arbitrary definition of responsiveness.

SUMMARY

The Vigileo™/FloTrac™ system (Edwards Lifesciences, Irvine, CA) is based on the analysis of the systemic arterial pressure wave without external calibration to continuously monitor cardiac output (CO) and SVV .It has been shown that SVV-FloTrac is a good indicator of fluid responsiveness by various studies conducted in cardiac patients[18,41] ,abdominal procedures[4,48] and in critically ill patients on mechanical ventilator[15]. The aim of this study was to assess whether SVV can serve as a predictor of fluid responsiveness in patients undergoing elective abdominal surgery and to compare its predictive value to the CVP and to commonly measured hemodynamic variables like heart rate, MAP, Systolic, diastolic blood pressure.

Twenty five patients of ASA PS 1/II who underwent elective abdominal surgeries were included in the study. A total of 150 volume loading steps (VLS) were performed of which 75 was volume responsive and 75 was nonresponsive. Comparison of the various hemodynamic variables before and after fluid loading were statistically analysed.

Our observations were

- There was correlation between the change in SV and the values of SVV. No correlation was found between the changes in SV and the values of the CVP.
- The change in SVV was pronounced in responders in comparison to non responders. But the change in CVP were not statistically significant in responders and non responders.
- Hemodynamic variable Before fluid loading, SVV (>13%)were significantly higher and CVP were significantly lower in Responders than in Non Responders.
- The area under the curve for SVV was Statistically more than those for CVP.
- MAP,DBP,SBP were also found to be predictors with less area under the curve in ROC curves when compared to SVV.
- The optimal threshold values given by ROC for SVV was 10.5%. Thus if a patient had a SVV value of more than 10.5% he was very likely to be responsive to a subsequent volume load by increasing his stroke volume by 5% with a sensitivity of 92 % and specificity of 64%.

CONCLUSIONS

This prospective study demonstrates that Stroke volume variation is a reliable predictor of fluid responsiveness in the setting of major abdominal surgery when compared to the central venous pressure, though central venous pressure is used for current intraoperative fluid management.

PROFORMA

NAME: DATE:

AGE/SEX: IP NO:

HEIGHT: WEIGHT: BSA:

DIAGNOSIS: START OF SURGERY:

SURGERY: END OF SURGERY:

ASA: COMORBID CONDITIONS:

INFORMED CONSENT:

MONITORS: PRE OP

ECG: SPO2: HR: BP:

PREMED:

INJ GLYCOPYRROLATE: INJ MIDAZOLAM:

INJ FENTANYL:

EPIDURAL LEVEL:

ARTERIAL LINE:

INTERNAL JUGULAR VEIN CANNULATION:

INDUCTION:

INJ PROPOFOL: INJ ATRACURIUM:

INTUBATION:

INTRA OP:

HR:

BP:

SPO2:

VLS	HR		SBP		MAP		DBP		CO		SVV		CVP		SV		^SV
	PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST	Res/ NonRes

URINE OUTPUT:

BLOOD LOSS:

EXTUBATED/POSTOP VENTILATION:

REMARKS:

ANESTHESIOLOGIST SIGNATURE:

BIBLIOGRAPHY

1. Bendjelid K & Romand JA. Fluid responsiveness in mechanically ventilated patients: a review of indices used in intensive care. Intensive Care Medicine 2003; 29: 352–360.

2. Berkenstadt H, Friedman Z, Preisman S et al. Pulse pressure and stroke volume variations during severe haemorrhage in ventilated dogs. British Journal of Anaesthesia 2005; 94: 721–726.

3. *Berkenstadt H, Margalit N, Hadani M, Friedman Z, Segal E, Villa Y, Perel A. Stroke volume variation as a predictor of fluid responsiveness in patients undergoing brain surgery.* Anesth Analg 2001;92:984–*9.*

4. *Biais M, Nouette-Gaulain K, Cottenceau V, Revel P, Sztark F. Uncalibrated pulse contour derived stroke volume variation predicts fluid responsiveness in mechanically ventilated patients undergoing liver transplantation.* Br J Anaesth 2008;101:761–*8*

5. Braunwald E, Sonnenblick EH, Ross J. Mechanisms of cardiac contraction and relaxation. In: Braunwald E (ed.).*HeartDisease*. W.B.Saunders Company: Philadelphia, PA, 1988, pp. 383–425.

6. Button D, Weibel L, Reuthebuch O, et al. *Clinical evaluation of the FloTrac/Vigileo system and two established continuous cardiac output monitoring devices in patients undergoing cardiac surgery. Br J Anaesth 2007;99:329-36.*

7. *Cannesson M, Musard H, Desebbe O, Boucau C, Simon R, Henaine R, Lehot JJ. The ability of stroke volume variations*

obtained with Vigileo/FloTrac system to monitor fluid responsiveness in mechanically ventilated patients. Anesth Analg 2009;108:513–*7.*

8. Charron C, Fessenmeyer C, Cosson C et al. The influence of tidal volume on the dynamic variables of fluid responsiveness in critically ill patients. Anesthesia and Analgesia 2006; 102: 1511–1517.

9. Coudray A, Romand JA, Treggiari M & Bendjelid K. Fluid responsiveness in spontaneously breathing patients: a review of indexes used in intensive care. Critical Care Medicine 2005.

10. Dalibon N, Schlumberger S, Saada M et al. Haemodynamic assessment of hypovolaemia under general anaesthesia in pigs submitted to graded haemorrhage and retransfusion. British Journal of Anaesthesia 1999; 82: 97–103.

11. De Backer D, Heenen S, Piagnerelli M, Koch M, Vincent JL. Pulse pressure variations to predict fluid responsiveness: influence of tidal volume. *Intensive Care Med* 2005;31:517-23.

12. De Backer D, Taccone FS, Holsten R, Ibrahimi F, Vincent JL Influence of respiratory rate on **stroke volume variation** in mechanically ventilated patients..Anesthesiology. 2009 May;110(5):1092-7.

13. Derichard A, Robin E,Grocott MP, Mythen MG, Gan TJBritish journal of anesthesia 2009 Nov;103(5):678-84. Epub 2009 Sep 29. Automated pulse pressure and stroke volume variations from radial artery: evaluation during major abdominal surgery**.**

14. E. B. Fonseca, D. A. Otsuki, D. T. Fantoni, F. Bliacheriene and J. O. C. Auler (2008). Comparative study of pressure- and volume-controlled ventilation on pulse pressure variation in a model of hypovolaemia in rabbits. European Journal of Anaesthesiology, 25 , pp 388-394.

15. Feissel M, Michard F, Mangin I, et al. Respiratory changes in aortic blood velocity as an indicator of fluid responsiveness in ventilated patients with septic shock. Chest 2001; 119: 867–73.

16. Goedje O, Hoeke K, Lichtwarck-Aschoff M et al. Continuous cardiac output by femoral arterial thermodilution calibrated pulse contour analysis: comparison with pulmonary arterial thermodilution. Critical Care Medicine 1999; 27: 2407–2412.

17. Heenen S, De Backer D, Vincent JLCritical care 2006 10(4):R102.How can the response to volume expansion in patients with spontaneous respiratory movements be predicted?.

18. Hofer CK, Muller SM, Furrer L, Klaghofer R, Genoni M, Zollinger A. Stroke volume and pulse pressure variation for prediction of fluid responsiveness in patients undergoing off-pump coronary artery bypass grafting. *Chest.* 2005;**128**:848–854.

19. *Hofer CK, Senn A, Weibel L, Zollinger A. Assessment of stroke volume variation for prediction of fluid responsiveness using the modified FloTrac and PiCCOplus system.* Crit Care 2008;12:R82

20. K. Bendjelid and J. A. Romand, “Fluid responsiveness in mechanically ventilated patients: a review of indices used in

intensive care," *Intensive Care Medicine*, vol. 29, no. 3, pp. 352–360, 2003.

21. Kubitz JC, Annecke T, Forkl S, Kemming GI, Kronas N, Goetz AE, Reuter DA.BJA2007 May;98(5):591-7.Validation of pulse contour derived stroke volume variation during modifications of cardiac afterload.

22. Kumar A, Anel R, Bunnell E et al. Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. Critical Care Medicine 2004; 32: 691–699.

23. Magder S. Clinical usefulness of respiratory variations in arterial pressure. American Journal of Respiratory and Critical CareMedicine 2004; 169: 151–155.

24. *Manecke GR. Edwards FloTrac sensor and Vigileo monitor: easy, accurate, reliable cardiac output assessment using the arterial pulse wave.* Expert Rev Med Devices 2005*;2:*523–*7.*

25. Manecke GR Jr, Auger WR . *Cardiac output determination from the arterial pressure wave: clinical testing of a novel algorithm that does not require calibration. J Cardiothorac Vasc Anesth 2007;21:3-7.*

26. Marik PE, Baram M & Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. Chest 2008; 134: 172–178.

27. Marik PE, Cavallazzi R, Vasu T, *et al*. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients. A systematic review of the literature. *CritCare Med* 2009; 37: 2642–7.

28. Mayer J, Boldt J, Schollhorn T, Rohm KD, Mengistu AM, Suttner S. Semi-invasive monitoring of cardiac output by a new device using arterial pressure waveform analysis: a comparison with intermittent pulmonary artery thermodilution in patients undergoing cardiac surgery. *Br J Anaesth.* 2007;**98**:176–182. doi: 10.1093/bja/ael341.

29. McNeil BJ.Radiology1982 Apr;143(1):29-36.The meaning and use of the area under a receiver operating characteristic (ROC) curve.Hanley JA.

30. Michard F & Teboul JL. Using heart-lung interactions to assess fluid responsiveness during mechanical ventilation. Critical Care 2000; 4: 282–289.

31. Michard F, Boussat S, Chemla D, Anguel N, Mercat A, Lecarpentier Y, Richard C, Pinsly MR, Teboul JL: **Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure.** *Am J Respir Crit Care Med* 2000, **162:**134-138.

32. Mitchell JR, Whitelaw WA, Sas R, et al. RV filling modulates LV function by direct ventricular interaction during mechanical ventilation. Am J Physiol 2005;289:H549–H557.

33. Monnet X, Teboul JL. Volume responsiveness. *Curr Opin Crit Care*. 2007;**13**:549–53.

34. **Miller's Anesthesia,7th Edition.** By Ronald D. Miller, M.D. , Lars I. Eriksson, M.D., Ph.D., Lee A. Fleisher, M.D., Jeanine P. Wiener-Kronish, M.D., and William L. Young, M.D. Philadelphia, Churchill Livingstone, 2009. 1268-1321

35. Micah ,H. Liu , M.R. Konia , Z. Li , N.W. Fleming **The Comparison of Stroke Volume Variation and Arterial Pressure Based Cardiac Output with Standard Hemodynamic Measurements during Cardiac Surgery** - Internet journal of anesthesiology vol 22 ;2010

36. Nixon JV, Murray RG, Leonard PD, *et al*. Effect of large variations in preload on left ventricular characteristics in normal subjects.*Circulation* 1982; 65: 698–703.

37. Osman D, Ridel C, Ray P et al. Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge. Critical Care Medicine 2007; 35: 64–68.

38. *Perioperative fluid management and clinical outcomes in adults. Anesth Analg 2005;100:1093-106.*

39. Pinsky MR, Payen D: **Functional hemodynamic monitoring.** *Crit Care* 2005, **9:**566-572.

40. Preisman S, Kogan S, Berkenstadt H, et al. *Predicting fluid responsiveness in patients undergoing cardiac surgery: functional haemodynamic parameters including the respiratory systolic*

variation test and static preload indicators. Br J Anaesth 2005;95:746-55.

41. Renner J, Cavus E, Meybohm P et al. Pulse pressure variation and stroke volume variation during different loading conditions in a paediatric animal model. Acta Anaesthesiologica Scandinavica 2008; 52: 374–380.

42. *Reuter DA, Felbinger TW, Schmidt C, Kilger E, Goedje O, Lamm P, Goetz AE. Stroke volume variations for assessment of cardiac responsiveness to volume loading in mechanically ventilated patients after cardiac surgery.* Intensive Care Med 2002*;*28*:*392*–8.*

43. Reuter DA, Bayerlein J, Goepfert MS, et al. Influence of tidal volume on left ventricular stroke volume variation measured by pulse contour analysis in mechanically ventilated patients. *Intensive Care Med* 2003*;*29*:*476-80.

44. Reuter DA, Kirchner A, Felbinger TW, Weis FC, Kilger E, Lamm P, Goetz AE. Usefulness of left ventricular stroke volume variation to assess fluid responsiveness in patients with reduced cardiac function. *Crit Care Med.* 2003;**31**:1399–1404.

45. Sander M, Spies CD, Foer A, von Heymann C et al Cardiac output measurement by arterial waveform analysis in cardiac surgery--a comparison of measurements derived from waveforms of the radial artery versus the ascending aorta. J Int Med Res. 2008 May-Jun;36(3):414-9.

46. Vincent JL & Weil MH. Fluid challenge revisited. Critical Care Medicine 2006; 34: 1333–1337.

47. Hiroshi Yamaguchi, Seiji Watanabe, Izumi Harukuni, and Yoshihiro Hamaya**Effective Doses of Epidural Morphine for Relief of Postcholecystectomy Pain** Anesth Analg January 1991 72:80-83

48. Zimmermann M, Feibicke T, Keyl C, Prasser C, Moritz S, Graf BM, Wiesenack C.European journal anaesthesiology 2010 Jun;27(6):555-61.Accuracy of stroke volume variation compared with pleth variability index to predict fluid responsiveness in mechanically ventilated patients undergoing major surgery.

MASTER CHART

S.NO	VLS	HR		SYSTOLIC BP		DIASTOLIC BP		MAP		CVP		CHANGE IN
		PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST	CVP%
1	1	119	116	104	115	60	58	75	77	9	9	0.00%
1	2	104	96	106	112	59	62	75	79	8	8	0.00%
1	3	112	108	98	106	57	63	71	77	8	9	0.00%
1	4	116	108	115	120	58	65	77	83	9	9	0.00%
1	5	96	94	112	114	62	64	79	81	8	8	0.00%
1	6	108	103	106	109	63	64	77	79	8	9	12.50%
2	7	77	73	93	106	50	61	64	76	6	6	0.00%
2	8	67	65	104	108	53	58	70	75	7	7	0.00%
2	9	69	67	108	110	58	60	75	77	6	7	16.67%
2	10	73	67	106	108	50	53	69	71	6	6	0.00%
2	11	67	66	112	115	60	64	77	81	8	8	0.00%
2	12	65	64	115	117	64	67	81	84	8	8	0.00%
3	13	77	78	121	127	60	61	80	83	8	8	0.00%
3	14	98	91	98	105	66	68	77	80	8	8	0.00%
3	15	81	80	110	113	65	65	80	81	8	8	0.00%
3	16	91	88	105	107	68	69	80	82	8	8	0.00%
3	17	78	72	127	128	61	68	83	88	8	9	12.50%
3	18	86	81	104	110	63	65	77	80	8	8	0.00%
4	19	95	91	91	124	46	62	61	83	8	8	0.00%
4	20	74	71	109	112	63	65	78	81	8	8	0.00%
4	21	77	76	107	114	58	62	74	79	7	7	0.00%
4	22	82	81	114	117	60	61	78	80	7	8	14.29%
4	23	85	84	108	110	56	58	73	75	8	8	0.00%
4	24	112	91	99	108	54	61	69	77	7	7	0.00%
5	25	78	74	100	109	52	63	68	78	7	8	14.29%

S.NO	VLS	HR		SYSTOLIC BP		DIASTOLIC BP		MAP		CVP		CHANGE IN
		PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST	CVP%
5	26	91	90	124	122	62	63	83	83	7	8	14.29%
5	27	89	85	96	108	54	56	68	73	8	8	0.00%
5	28	88	80	96	101	54	64	68	76	8	9	12.50%
5	29	91	87	108	114	61	60	77	78	8	8	0.00%
5	30	80	79	101	105	64	68	76	80	9	9	0.00%
6	31	83	73	104	121	64	70	77	87	9	10	11.11%
6	32	75	73	118	119	67	68	84	85	10	10	0.00%
6	33	62	62	105	110	63	69	77	83	10	10	0.00%
6	34	73	70	121	124	70	72	87	89	10	10	0.00%
6	35	62	66	110	108	69	69	83	82	10	10	0.00%
6	36	54	54	108	109	62	63	77	78	11	11	0.00%
7	37	89	84	101	107	63	68	76	81	9	9	0.00%
7	38	70	67	124	125	72	72	89	90	10	10	0.00%
7	39	67	65	114	117	67	68	83	84	10	10	0.00%
7	40	93	88	105	112	70	75	82	92	9	9	0.00%
7	41	65	63	117	118	68	68	84	85	10	10	0.00%
7	42	79	75	117	118	66	67	83	84	10	10	0.00%
8	43	95	93	95	105	68	70	77	85	8	9	12.50%
8	44	88	73	112	121	75	70	87	92	9	10	11.11%
8	45	62	61	105	107	63	64	77	83	10	10	0.00%
8	46	84	82	107	109	68	69	81	82	9	9	0.00%
8	47	61	67	107	106	64	61	78	81	10	10	0.00%
8	48	61	63	99	100	59	60	72	78	10	10	0.00%
9	49	85	84	101	109	70	72	80	84	8	8	0.00%
9	50	92	88	94	102	65	68	75	79	8	8	0.00%
9	51	86	85	108	109	69	71	82	84	9	9	0.00%

S.NO	VLS	HR		SYSTOLIC BP		DIASTOLIC BP		MAP		CVP		CHANGE IN
		PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST	CVP%
9	52	78	76	101	102	70	69	80	80	9	9	0.00%
9	53	88	86	102	108	68	69	79	82	8	8	0.00%
9	54	76	75	102	106	69	72	80	83	9	9	0.00%
10	55	115	107	92	97	54	59	67	72	7	7	0.00%
10	56	114	110	96	99	57	60	70	73	7	7	0.00%
10	57	107	102	93	99	54	58	67	72	8	8	0.00%
10	58	107	102	97	100	59	61	72	74	7	7	0.00%
10	59	110	108	99	101	60	64	73	76	7	8	14.29%
10	60	102	100	99	109	58	62	72	78	8	9	12.50%
11	61	91	83	116	122	61	63	79	83	8	8	0.00%
11	62	85	82	116	118	64	65	81	83	8	8	0.00%
11	63	83	81	122	124	63	64	83	84	8	8	0.00%
11	64	101	92	98	107	61	65	73	79	9	9	0.00%
11	65	86	84	112	114	61	64	78	81	9	9	0.00%
11	66	79	82	108	114	61	60	77	78	9	9	0.00%
12	67	96	93	98	103	56	62	70	76	8	8	0.00%
12	68	97	92	100	110	53	58	69	75	8	8	0.00%
12	69	97	95	105	107	59	61	74	76	8	8	0.00%
12	70	108	100	101	110	57	62	72	78	8	8	0.00%
12	71	92	90	110	112	58	59	75	77	9	9	0.00%
12	72	96	94	114	116	67	70	83	85	8	8	0.00%
13	73	104	97	97	105	54	59	68	74	8	8	0.00%
13	74	99	96	109	114	64	67	79	83	9	9	0.00%
13	75	100	98	110	113	62	63	78	80	7	7	0.00%
13	76	99	92	100	109	58	63	72	78	7	8	14.29%
13	77	93	91	103	106	62	65	76	79	7	7	0.00%

S.NO	VLS	HR		SYSTOLIC BP		DIASTOLIC BP		MAP		CVP		CHANGE IN
		PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST	CVP%
13	78	92	90	109	111	63	66	78	81	7	7	0.00%
14	79	88	85	110	116	59	64	76	81	8	8	0.00%
14	80	91	86	102	106	62	66	75	79	8	8	0.00%
14	81	82	81	114	117	60	61	78	80	8	8	0.00%
14	82	88	86	109	112	58	61	75	78	9	9	0.00%
14	83	86	83	106	108	66	67	79	81	8	9	12.50%
14	84	92	88	107	109	65	67	79	81	9	9	0.00%
15	85	69	66	112	116	64	68	80	84	9	9	0.00%
15	86	62	61	117	120	69	70	85	87	10	10	0.00%
15	87	71	65	105	115	68	70	80	85	10	10	0.00%
15	88	66	64	116	118	68	69	84	85	9	9	0.00%
15	89	65	64	115	119	70	69	85	86	8	9	12.50%
15	90	65	62	109	117	66	69	80	85	9	9	0.00%
16	91	71	69	112	115	54	58	73	77	9	9	0.00%
16	92	68	67	116	117	68	69	84	85	10	10	0.00%
16	93	68	64	116	121	69	71	85	88	9	10	11.11%
16	94	69	67	115	120	58	62	77	81	9	9	0.00%
16	95	73	71	114	118	59	61	77	80	9	9	0.00%
16	96	67	66	113	115	69	70	84	85	8	8	0.00%
17	97	104	100	99	107	63	66	75	80	8	8	0.00%
17	98	110	98	94	102	64	68	74	79	8	8	0.00%
17	99	85	81	112	116	62	64	79	81	8	8	0.00%
17	100	98	95	102	108	68	69	79	82	8	9	12.50%
17	101	84	82	105	109	68	69	80	82	8	8	0.00%
17	102	101	95	101	107	67	69	78	82	8	9	12.50%
18	103	88	85	109	112	59	62	76	79	8	8	0.00%

S.NO	VLS	HR		SYSTOLIC BP		DIASTOLIC BP		MAP		CVP		CHANGE IN
		PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST	CVP%
18	104	89	84	97	105	66	68	76	80	8	8	0.00%
18	105	95	92	107	109	69	70	82	83	8	8	0.00%
18	106	91	86	100	106	60	64	73	78	8	8	0.00%
18	107	100	98	107	110	66	69	80	83	8	8	0.00%
18	108	86	84	106	108	64	65	78	79	9	10	11.11%
19	109	69	68	111	116	65	68	80	84	10	10	0.00%
19	110	66	65	115	118	63	67	80	84	10	10	0.00%
19	111	71	70	118	121	61	62	80	82	9	9	0.00%
19	112	69	67	108	113	67	69	81	84	9	9	0.00%
19	113	65	65	118	120	67	68	84	85	10	10	0.00%
19	114	64	63	121	123	71	70	88	88	9	10	11.11%
20	115	109	102	101	109	64	68	76	82	9	9	0.00%
20	116	99	94	104	110	65	70	78	83	9	9	0.00%
20	117	100	98	107	110	62	63	77	79	9	9	0.00%
20	118	93	91	114	118	70	73	85	88	9	9	0.00%
20	119	82	80	111	112	72	73	85	86	8	9	12.50%
20	120	91	90	118	119	73	74	88	89	8	8	0.00%
21	121	67	66	112	118	69	72	83	87	8	8	0.00%
21	122	94	92	110	112	70	71	83	85	9	9	0.00%
21	123	75	74	110	111	80	82	90	92	9	9	0.00%
21	124	102	94	109	108	68	69	82	82	9	9	0.00%
21	125	119	104	92	105	54	60	67	75	8	9	12.50%
21	126	109	100	98	107	58	62	71	77	9	9	0.00%
22	127	79	75	108	110	78	80	88	90	9	9	0.00%
22	128	84	79	105	109	69	71	81	84	9	9	0.00%
22	129	104	98	105	108	60	62	75	77	8	9	12.50%

S.NO	VLS	HR		SYSTOLIC BP		DIASTOLIC BP		MAP		CVP		CHANGE IN
		PRE	POST	PRE	POST	PRE	POST	PRE	POST	PRE	POST	CVP%
22	130	79	72	109	110	71	71	84	84	8	8	0.00%
22	131	91	82	106	111	69	72	81	85	9	9	0.00%
22	132	66	65	118	119	72	73	87	88	8	8	0.00%
23	133	102	94	94	102	58	63	70	76	9	9	0.00%
23	134	101	96	106	108	61	62	76	77	9	9	0.00%
23	135	95	91	104	108	64	67	77	81	9	9	0.00%
23	136	90	88	109	111	57	59	74	76	9	9	0.00%
23	137	104	95	99	108	60	63	73	78	9	9	0.00%
23	138	95	92	108	111	63	65	78	80	9	9	0.00%
24	139	91	87	101	106	58	60	72	75	9	9	0.00%
24	140	104	99	99	108	62	68	74	81	9	10	11.11%
24	141	91	89	108	110	67	68	81	82	9	9	0.00%
24	142	87	84	106	108	60	61	75	77	9	9	0.00%
24	143	89	86	105	107	59	60	74	76	9	10	11.11%
24	144	96	90	106	109	53	57	71	74	10	10	0.00%
25	145	109	101	96	106	58	61	71	76	9	9	0.00%
25	146	92	88	105	108	58	63	74	78	9	9	0.00%
25	147	94	91	102	106	63	64	76	78	9	9	0.00%
25	148	88	86	108	109	63	65	78	80	9	9	0.00%
25	149	94	89	101	105	54	59	70	74	8	9	12.50%
25	150	99	96	108	109	68	69	81	82	9	9	0.00%

S.NO	VLS	SVV		CHANGE IN	CO		SV		% CHANGE	RESPONDERS/ NON RESPONDERS
		PRE	POST	SVV %	PRE	POST	PRE	POST		
1	1	21	13	-38.10%	4.76	5.80	40	50	25.00%	RES
1	2	15	11	-26.67%	5.41	5.57	52	58	11.54%	RES
1	3	17	11	-35.29%	6.16	6.26	55	58	5.45%	RES
1	4	13	11	-15.38%	5.80	5.62	50	52	4.00%	NS
1	5	11	9	-18.18%	5.57	5.64	58	60	3.45%	NS
1	6	11	10	- 9.09%	6.26	6.18	58	60	3.45%	NS
2	7	15	9	-40.00%	4.47	4.96	58	68	17.24%	RES
2	8	14	11	-21.43%	4.09	4.55	61	70	14.75%	RES
2	9	11	8	-27.27%	4.83	4.89	70	73	4.29%	NS
2	10	9	8	-11.11%	4.96	4.76	68	71	4.41%	NS
2	11	13	8	-38.46%	4.22	4.49	63	68	7.94%	RES
2	12	8	7	-12.50%	4.42	4.48	68	70	2.94%	NS
3	13	9	6	-33.33%	5.85	6.32	76	81	6.58%	RES
3	14	11	8	-27.27%	5.49	5.73	56	63	12.50%	RES
3	15	9	7	-22.22%	5.18	5.36	64	67	4.69%	NS
3	16	8	7	-12.50%	5.73	5.72	63	65	3.17%	NS
3	17	6	6	0.00%	6.32	5.98	81	83	2.47%	NS
3	18	13	9	-30.77%	4.90	5.18	57	64	12.28%	RES
4	19	11	9	-18.18%	5.13	6.28	54	69	27.78%	RES
4	20	11	9	-18.18%	5.03	5.04	68	71	4.41%	NS
4	21	11	9	-18.18%	5.47	5.78	71	76	7.04%	RES
4	22	9	7	-22.22%	5.82	5.91	71	73	2.82%	NS
4	23	9	8	-11.11%	5.36	5.46	63	65	3.17%	NS
4	24	15	8	-46.67%	5.26	6.01	47	66	40.43%	RES
5	25	21	11	-47.62%	4.21	5.03	54	68	25.93%	RES

S.NO	VLS	SVV		CHANGE IN	CO		SV		% CHANGE	RESPONDERS/ NON RESPONDERS
		PRE	POST	SVV %	PRE	POST	PRE	POST		
5	26	9	8	-11.11%	6.28	6.48	69	72	4.35%	NS
5	27	15	9	-40.00%	4.90	5.36	55	63	14.55%	RES
5	28	14	9	-35.71%	4.58	5.28	52	66	26.92%	RES
5	29	8	7	-12.50%	6.01	5.92	66	68	3.03%	NS
5	30	9	7	-22.22%	5.28	5.45	66	69	4.55%	NS
6	31	18	13	-27.78%	3.98	4.09	48	56	16.67%	RES
6	32	9	8	-11.11%	5.40	5.33	72	73	1.39%	NS
6	33	12	11	-8.33%	3.53	4.09	57	66	15.79%	RES
6	34	13	11	-15.38%	4.09	4.27	56	61	8.93%	RES
6	35	11	9	-18.18%	4.09	4.42	66	67	1.52%	NS
6	36	11	10	-9.09%	3.73	3.89	69	72	4.35%	NS
7	37	11	9	-18.18%	4.81	4.96	54	59	9.26%	RES
7	38	11	9	-18.18%	4.27	4.29	61	64	4.92%	NS
7	39	10	8	-20.00%	4.02	4.23	60	65	8.33%	RES
7	40	11	9	-18.18%	4.19	4.58	45	52	15.56%	RES
7	41	8	8	0.00%	4.23	4.28	65	68	4.62%	NS
7	42	10	9	-10.00%	5.37	5.40	68	72	5.88%	RES
8	43	13	11	-15.38%	3.71	4.19	39	45	15.38%	RES
8	44	9	7	-22.22%	4.58	3.94	52	54	3.85%	NS
8	45	12	11	-8.33%	3.53	3.97	57	65	14.04%	RES
8	46	9	8	-11.11%	4.96	5.00	59	61	3.39%	NS
8	47	11	10	-9.09%	3.97	4.56	65	68	4.62%	NS
8	48	9	9	0.00%	4.27	4.54	70	72	2.86%	NS
9	49	9	9	0.00%	5.44	5.46	64	65	1.56%	NS
9	50	13	10	-23.08%	5.34	5.63	58	64	10.34%	RES
9	51	10	9	-10.00%	5.85	5.87	68	69	1.47%	NS
9	52	9	8	-11.11%	4.99	5.17	64	68	6.25%	RES

S.NO	VLS	SVV		CHANGE IN	CO		SV		% CHANGE	RESPONDERS/ NON RESPONDERS
		PRE	POST	SVV %	PRE	POST	PRE	POST		
9	53	11	10	-9.09%	5.63	5.85	64	68	6.25%	RES
9	54	8	7	-12.50%	5.17	5.18	68	69	1.47%	NS
10	55	15	11	-26.67%	4.72	5.24	41	49	19.51%	RES
10	56	14	10	-28.57%	5.02	5.28	44	48	9.09%	RES
10	57	12	9	-25.00%	5.24	5.51	49	54	10.20%	RES
10	58	11	9	-18.18%	5.24	5.20	49	51	4.08%	NS
10	59	10	8	-20.00%	5.28	5.40	48	50	4.17%	NS
10	60	9	8	-11.11%	5.51	5.60	54	56	3.70%	NS
11	61	13	10	-23.08%	5.73	5.64	63	68	7.94%	RES
11	62	9	8	-11.11%	5.44	5.41	64	66	3.13%	NS
11	63	10	9	-10.00%	5.64	5.75	68	71	4.41%	NS
11	64	15	11	-26.67%	5.86	5.98	58	65	12.07%	RES
11	65	9	8	-11.11%	6.28	6.22	73	74	1.37%	NS
11	66	9	7	-22.22%	5.37	5.90	68	72	5.88%	RES
12	67	10	8	-20.00%	6.14	6.32	64	68	6.25%	RES
12	68	16	11	-31.25%	5.43	5.70	56	62	10.71%	RES
12	69	11	9	-18.18%	6.21	6.27	64	66	3.13%	NS
12	70	15	10	-33.33%	6.26	6.10	58	61	5.17%	RES
12	71	11	9	-18.18%	5.70	5.76	62	64	3.23%	NS
12	72	10	9	-10.00%	6.53	6.67	68	71	4.41%	NS
13	73	18	11	-38.89%	5.93	6.21	57	64	12.28%	RES
13	74	14	10	-28.57%	6.24	6.53	63	68	7.94%	RES
13	75	10	9	-10.00%	6.10	6.17	61	63	3.28%	NS
13	76	13	10	-23.08%	5.45	5.52	55	60	9.09%	RES
13	77	8	7	-12.50%	6.32	6.46	68	71	4.41%	NS
13	78	10	8	-20.00%	5.52	5.58	60	62	3.33%	NS
14	79	12	9	-25.00%	5.19	5.44	59	64	8.47%	RES

S.NO	VLS	SVV		CHANGE IN	CO		SV		% CHANGE	RESPONDERS/ NON RESPONDERS
		PRE	POST	SVV %	PRE	POST	PRE	POST		
14	80	13	9	-30.77%	5.46	5.50	60	64	6.67%	RES
14	81	10	9	-10.00%	5.82	5.91	71	73	2.82%	NS
14	82	11	9	-18.18%	6.07	6.28	69	73	5.80%	RES
14	83	9	7	-22.22%	5.50	5.56	64	67	4.69%	NS
14	84	11	9	-18.18%	5.98	5.90	65	67	3.08%	NS
15	85	14	9	-35.71%	4.97	5.15	72	78	8.33%	RES
15	86	11	8	-27.27%	4.71	4.76	76	78	2.63%	NS
15	87	12	8	-33.33%	5.18	5.14	73	79	8.22%	RES
15	88	9	8	-11.11%	5.15	5.06	78	79	1.28%	NS
15	89	8	7	-12.50%	5.14	5.12	79	80	1.27%	NS
15	90	15	11	-26.67%	4.62	4.71	71	76	7.04%	RES
16	91	13	10	-23.08%	5.04	5.24	71	76	7.04%	RES
16	92	10	9	-10.00%	5.17	5.23	76	78	2.63%	NS
16	93	13	9	-30.77%	5.10	5.06	75	79	5.33%	RES
16	94	10	8	-20.00%	5.24	5.23	76	78	2.63%	NS
16	95	15	11	-26.67%	5.26	5.54	72	78	8.33%	RES
16	96	9	8	-11.11%	5.16	5.21	77	79	2.60%	NS
17	97	17	11	-35.29%	5.41	5.60	52	56	7.69%	RES
17	98	16	10	-37.50%	5.61	5.49	51	56	9.80%	RES
17	99	9	7	-22.22%	5.02	4.94	59	61	3.39%	NS
17	100	10	7	-30.00%	5.49	5.51	56	58	3.57%	NS
17	101	11	9	-18.18%	4.87	4.92	58	60	3.45%	NS
17	102	15	11	-26.67%	5.35	5.61	53	59	11.32%	RES
18	103	13	9	-30.77%	4.66	5.02	53	59	11.32%	RES
18	104	14	11	-21.43%	4.81	4.87	54	58	7.41%	RES
18	105	11	9	-18.18%	5.61	5.52	59	60	1.69%	NS
18	106	18	11	-38.89%	5.01	5.25	55	61	10.91%	RES

S.NO	VLS	SVV		CHANGE IN	CO		SV		% CHANGE	RESPONDERS/ NON RESPONDERS
		PRE	POST	SVV %	PRE	POST	PRE	POST		
18	107	11	9	-18.18%	5.60	5.68	56	58	3.57%	NS
18	108	11	8	-27.27%	5.25	5.38	61	64	4.92%	NS
19	109	15	10	-33.33%	4.90	5.17	71	76	7.04%	RES
19	110	17	13	-23.53%	4.62	5.07	70	78	11.43%	RES
19	111	11	9	-18.18%	5.61	5.67	79	81	2.53%	NS
19	112	13	9	-30.77%	4.83	5.16	70	77	10.00%	RES
19	113	13	10	-23.08%	5.07	5.20	78	80	2.56%	NS
19	114	9	7	-22.22%	5.06	5.10	79	81	2.53%	NS
20	115	15	11	-26.67%	5.89	6.12	54	60	11.11%	RES
20	116	13	9	-30.77%	5.74	5.83	58	62	6.90%	RES
20	117	9	8	-11.11%	5.30	5.39	53	55	3.77%	NS
20	118	12	9	-25.00%	5.49	6.01	59	66	11.86%	RES
20	119	9	7	-22.22%	5.00	5.04	61	63	3.28%	NS
20	120	9	7	-22.22%	6.01	6.12	66	68	3.03%	NS
21	121	12	8	-33.33%	4.56	4.75	68	72	5.88%	RES
21	122	9	8	-11.11%	5.83	5.98	62	65	4.84%	NS
21	123	11	9	-18.18%	5.10	5.18	68	70	2.94%	NS
21	124	11	10	-9.09%	6.12	5.83	60	62	3.33%	NS
21	125	18	11	-38.89%	5.00	5.62	42	54	28.57%	RES
21	126	13	9	-30.77%	5.23	5.30	48	53	10.42%	RES
22	127	15	11	-26.67%	4.90	5.10	62	68	9.68%	RES
22	128	11	8	-27.27%	5.38	5.37	64	68	6.25%	RES
22	129	11	8	-27.27%	5.62	5.49	54	56	3.70%	NS
22	130	8	7	-12.50%	5.37	5.11	68	71	4.41%	NS
22	131	13	9	-30.77%	5.10	5.00	56	61	8.93%	RES
22	132	8	7	-12.50%	4.75	4.75	72	73	1.39%	NS
23	133	13	8	-38.46%	5.20	5.45	51	58	13.73%	RES

S.NO	VLS	SVV		CHANGE IN	CO		SV		% CHANGE	RESPONDERS/ NON RESPONDERS
		PRE	POST	SVV %	PRE	POST	PRE	POST		
23	134	11	9	-18.18%	5.45	5.38	54	56	3.70%	NS
23	135	13	11	-15.38%	5.13	5.28	54	58	7.41%	RES
23	136	9	8	-11.11%	5.40	5.37	60	61	1.67%	NS
23	137	14	11	-21.43%	5.72	5.70	55	60	9.09%	RES
23	138	11	9	-18.18%	5.70	5.61	60	61	1.67%	NS
24	139	13	9	-30.77%	5.01	5.22	55	60	9.09%	RES
24	140	13	11	-15.38%	5.82	6.04	56	61	8.93%	RES
24	141	11	10	-9.09%	5.28	5.34	58	60	3.45%	NS
24	142	9	8	-11.11%	5.22	5.12	60	61	1.67%	NS
24	143	8	7	-12.50%	5.34	5.33	60	62	3.33%	NS
24	144	12	9	-25.00%	5.38	5.40	56	60	7.14%	RES
25	145	15	11	-26.67%	5.12	5.45	47	54	14.89%	RES
25	146	11	8	-27.27%	5.06	5.19	55	59	7.27%	RES
25	147	8	7	-12.50%	5.45	5.46	58	60	3.45%	NS
25	148	8	7	-12.50%	5.19	5.25	59	61	3.39%	NS
25	149	11	8	-27.27%	5.08	5.34	54	60	11.11%	RES
25	150	11	9	-18.18%	6.04	6.05	61	63	3.28%	NS

Key:

ASA - American Society of Anaesthesiologist
VLS - Volume loading step
CVP - Central Venous Pressure
SVV - Stroke Volume Variation
CO - Cardiac Output
RES - Responders
PRE - Before volume loading
HR - Heart Rate
SBP - Systolic Blood Pressure
DBP - Diastolic Blood Pressure
MAP - Mean Arterial Pressure
SV - Stroke Volume
NS - Non Responder
POST - After Volume Loading

S.NO	NAME	AGE	SEX	IP NO	ASA	DIAGNOSIS	PROCEDURE	HEIGHT	WEIGHT	BSA
1	MALAR	45	F	14017	2	CHOLEDOCHAL CYST	EXCISION/HJ	155	53	1.52
2	PONNAN	59	M	14998	2	CHOLEDOCHAL CYST	EXCISION/HJ	155	54	1.53
3	PRABHA	22	F	14992	1	CCP	FREY PROCEDURE	156	50	1.47
4	RAJAM	57	F	19296	2	DUODENAL GROWTH	WHIPPLE'S PROCEDURE	163	51	1.51
5	PANDI	30	F	22295	2	CCP	FREY PROCEDURE	154	53	1.51
6	THANIGAVEL	35	F	26396	2	CCP	FREY PROCEDURE	154	52	1.5
7	PREETHI	20	F	11620	1	CCP	FREY PROCEDURE	162	58	1.62
8	ARUL SELVI	35	F	27526	1	BILIARY STRICTURE	HEPATOJEJUNOSTOMY	160	56	1.58
9	IYAPPAN	25	M	23789	1	CCP	FREY PROCEDURE	164	60	1.66
10	MANOHARAN	40	M	15745	2	UNCINATE GROWTH	WHIPPLE'S PROCEDURE	163	53	1.55
11	SAVITHRI	39	F	16008	2	PERIAMPULLARY CARCINOMA	WHIPPLE'S PROCEDURE	154	52	1.5
12	SEETHA RAMAN	44	M	15140	1	CCP	FREY PROCEDURE	158	56	1.57
13	ASHWINI	27	F	17213	1	CCP	FREY PROCEDURE	155	56	1.56
14	NATESAN	40	M	22345	1	CCP	FREY PROCEDURE	164	62	1.69
15	JEYANTHI	32	F	23316	1	POST CHOLECYSTECTOMY LEAK	HEPATOJEJUNOSTOMY	157	54	1.54
16	VANAJA	49	F	19174	2	PERIAMPULLARY CARCINOMA	WHIPPLE'S PROCEDURE	158	57	1.59
17	MATHIVALAGAN	40	M	21587	1	CCP	FREY PROCEDURE	163	60	1.65
18	NAGARAJ	54	M	22543	2	PERIAMPULLARY CARCINOMA	WHIPPLE PROCEDURE	166	54	1.57
19	BALASUBRAMANIYAN	47	M	27211	2	PERIAMPULLARY CARCINOMA	WHIPPLE'S PROCEDURE	164	55	1.58
20	VEERAMMAL	40	F	14569	1	POST CHOLECYSTECTOMY STRICTURE	HEPATOJEJUNOSTOMY	157	51	1.49
21	BANUPRIYA	26	F	24933	1	CCP	FREY PROCEDURE	154	53	1.51

S.NO	NAME	AGE	SEX	IP NO	ASA	DIAGNOSIS	PROCEDURE	HEIGHT	WEIGHT	BSA
22	VIJAYAN	32	M	27212	2	PERIAMPULLARY CARCINOMA	TRIPLE BYPASS	162	58	1.62
23	MUNUSAMY	50	M	24310	2	CCP	FREY PROCEDURE	163	60	1.65
24	VIJAYAKUMARI	25	M	21189	2	CHOLEDOCHAL CYST	HEPATOJEJUNOSTOMY	158	57	1.59
25	SARAVANAN	19	M	29617	1	CCP	FREY PROCEDURE	165	61	1.68

நோயாளி தகவல் தாள்

ஸ்போரக் வால்யூம் வேரியேஷன் □S□r□□□ □□□□□ □ □□r□□□□□□ அறுவை சிகிச்சையின் போது செலுத்தப்படும் திரவத்தின் அளவை முன்கூட்டியே அறிவிக்கும் காரணி என்பதை பற்றிய ஆய்வு.

நோயாளிகளுக்கான தகவல் :

ஆராய்ச்சியின் நோக்கமும், ஆதாயங்களும் :

உங்கள் உறவினரை ஈடுபடுத்த திட்டமிடப்பட்டுள்ள இந்த மருத்துவ ஆய்வானது அறுவை சிகிச்சையின்போது செலது;தப்படும் திரவத்தின் அளவை முன்கூட்டியே அறிவிக்கும் காரணியாக ஸ்டோரக் வால்யூம் வேரியேஷன் □S□□□து என்பதை பற்றிய ஆய்வு.

பொதுவாக இத்தகைய அறுவை சிகிச்சையின்போது, நோயாளியின் சுவாசக் குழாயில் □Tr□□□□□□ சிறு டியூப் □E□d□□r□□□□□□ T□□□□ மூலம் மயக்க மருந்து கொடுக்கப்படும்ஙந. இன்டர்னல் ஜீகுலார் வெயின் என்னும் இரத்தக்குழாயானது □□□□r□□□ □□□□□□r □□□□□ மூளையில் இருந்து இருதயத்திற்கு செய்வதாகும். ரேடியல் ஆர்டரி □R□d□□ Ar□□r□□ என்பது கையின் மணிக்கட்டில் இருக்கும் இரத்தக்குழாய். இதன் இரண்டிலும் ஒரு மெல்– ய கதிட்டர் □C□□□□□□r□ செலுத்தப்பட்டு இயந்திரத்துடன் பொருத்தப்படும். இயந்திரத்தி– ருந்து ஸ்டோரக் வால்யூம் வேரியேஷன் □S□□□ மற்றும் சென்ட்ரல் வீனஸ் பிரஷர் □C□□r□□ □□□□□□ □r□□□□r□□ □C□□□ கணக்கிடப்படும். S□□ எனப்படுவது ரத்தத்தின் அளவு குறைவதை முத– ல் எடுத்துக்காட்டுவதாக திகழ்கிறது.

ஆய்வுமுறை :

இந்த ஆய்வில் உங்கள் உறவினருக்கு அறுவை சிகிச்சைக்கு செல்லும் முன் தூக்க மருந்து கொடுத்து அறைக்கு எடுத்துச் செல்லப்படுவார்கள். பின்னர் அறுவை அறையல் முதுகில் ஒரு சிறிய ஊசியின் மூலம் எபிடியூரல் கதிட்டர் □E□d□r□□C□□□□□r□ செலுத்தப்படும். இது அறுவை சிகிச்சை முடிந்த பிறகு வ– நீக்கும் மருந்தை செலுத்த பயன்படுவதாகும். மற்றும் □□□r□□□ □□□□□r □□□□□R□d□□Ar□□r□ ஆகியவற்றில் கதிட்டர் செலுத்தப்பட்டு இயந்திரத்துடன் பொருத்தப்படும். இதைக் கொண்டு அறுவை சிகிச்சை செய்யப்படுபவரின் இருதயத் துடிப்பு, ரத்தத்தின் அளவு, C□□□S□□ ஆகியவற்றை அறுவை சிகிச்சையின் போது தொடர்ந்து கண்காணிக்கப்படும். சிகிச்சைக்கு பின் மயக்கத்தி– ருந்து வெளியே கொண்டு வரப்பட்டு E□d□r□□□□□□T□□□ எடுக்கப்படும்.

உண்டாக கூடிய இடங்கள் :

அனைத்து மயக்க முறைகளுடன் இருப்பது போலவே இந்த முறையிலும் சில எதிர்பாரா இடர்கள் நடைபெறலாம். இந்த தூக்க மருந்துகள் பயன்படுத்தினால் இரத்த அழுத்தம் குறைவதற்கான வாய்ப்புள்ளது மற்றும் இருதய துடிப்பு குறையவும் வாய்ப்பு உள்ளது.

ஆய்வில் உங்கள் உரிமைகள் :

உங்கள் மருத்துவப் பதிவேடுகள் மிகவும் அந்தரங்கமாக வைத்துக் கொள்ளப்படும். இந்த ஆய்வின் முடிவுகள் அறிவியல் பத்திரிக்கைகளில் பிரசுரிக்கப்படலாம். ஆனால், பெயரை வெளியிடுவது மூலம் உங்கள் உறவினர் அயைாளம் காட்டப்படமாட்டார்கள். இந்த ஆய்வில் உங்கள் உறிவனரின் பங்கேற்பு தன்னிச்சையானது மற்றும் காரணங்கள் எதையும் கூறாமலேயே நீங்கள் இந்த ஆய்வி– ருந்து எந்த ஒரு நேரத்திலும் விலகிக் கொள்ளலாம். எப்படி இருந்தாலும் உங்கள் உறவினருக்கு தகுந்த மயக்கமருந்து கொடுத்து அறுவை சிகிச்சை செய்யப்படும். பின்னர் தீவிர சிகிச்சைப் பிரிவில் கண்காணிக்கப்படுவார். இந்த ஆய்வில் ஏதேனும் பக்க விளைவுகள் ஏற்பட்டால் உங்கள் உறவினருக்கு முழு சிகிச்சை மருத்துவ குழுவினரால் அளிக்கப்படும்.

நாள் :

இடம் :

நோயாளியின் கையொப்பம்

இடது பெருவிரல் ரேகை

(மருத்துவரால் படித்து காட்டப்பட்டது).

சுய ஒப்புதல் படிவம்

ஆராய்ச்சி நிலையம் : அரசு ஸ்டான்– மருத்துவமனை

சென்னை – 600 001.

பங்கு பெறுபவரின் பெயர் :

பங்கு பெறுபவரின் எண் :

பங்கு பெறுபவர் இதனை ( ) குறிக்கவும்.

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப் பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது.

நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சாந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்கு பெறும் மருத்து என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின் படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய்க்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணிக்கு தெரிவிப்பேன் என உறுதி அளிக்கிறேன்.

இந்த ஆய்வில் எனக்கு இரத்தம், சிறுநீர், எக்ஸரே, ஸ்கேன் உட்பட அனைத்து பரிசோதனைகளையும் செய்து கொள்ள நான் முழு மனதுடன் சம்மதிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் :

கட்டைவிரல் ரேகை :

பங்கேற்பவரின் பெயர் :

மற்றும் விலாசம்

ஆய்வாளரின் கையொப்பம் :

ஆய்வாளரின் பெயர் :

இடம் :

தேதி :

INSTITUTIONAL ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Stroke volume variation as a prediction of fluid responsiveness in patients undergoing elective major abdominal Surgeries

Principal Investigator : Dr.K.J. Kaviya

Designation : PG in M.D(Anaes)

Department : Department of Anaesthesia
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 18.04.2011 at the Modernized Seminar Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate form the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

07/12/11

MEMBER SECRETARY,
IEC, SMC, CHENNAI

ABSTRACT

Stroke volume variation as a predictor for fluid responsiveness in patients undergoing elective major abdominal surgeries.

Introduction:

Stroke volume variation may be used as a continuous preload variable and in combination with the continuously measured cardiac output, the most important characteristics of cardiac function, allowing for optimal fluid management.

In patients undergoing major abdominal surgery, preoperative fasting, induction of general anesthesia, epidural analgesia and intraoperative bleeding may decrease intravascular volume, blood pressure, as a result leads to compromise perfusion of organs. Conventional hemodynamic variables, such as blood pressure, heart rate (HR), central venous pressure (CVP), and even pulmonary artery occlusion pressure (PAOP), are insensitive and sometimes misleading in the assessment of circulating blood volume. Measuring left ventricular (LV) end-diastolic area by transesophageal echocardiography (TEE), although considered to be the clinical "gold standard" for the estimation of preload, is limited to a small number of patients and is not routinely used in most operating rooms.

As an alternative to these static variables, assessment of stroke volume variation (SVV) has been used as a dynamic index to guide fluid therapy in patients receiving mechanical ventilation. The SVV are more pronounced during hypovolemia and the variation decreases if intravascular volume is restored, and it has shown to reliably predict changes in cardiac output.

AIM:

The aim of this study was to assess whether Stroke volume variation(SVV) can serve as a predictor of fluid responsiveness in patients undergoing elective major abdominal surgery and to compare its predictive value to the Central venous pressure (CVP)

Type of study: Observational study.

Inclusion criteria:

- Elective major abdominal surgery (intestine resection, gastric resection, Whipple procedure, frey procedure) .
- Both genders
- Age>18 years
- ASA PS I/II

Exclusion criteria:

- Patients under 18 years,
- Patients with severe aortic regurgitation,
- Patients with renal impairment
- Permanent cardiac arrhythmias,
- Patients undergoing emergency surgery were excluded from the study.

Study Materials:

IV cannula,Airway equipments.

Standard monitors.

Anesthesia ventilator.

Arterial line.

Central venous catheters

Vigileo flotrac monitor for SVV.

Study Methods:

Thirty patients of similar age group, weight and equal sex distribution will be included in the study

Informed written consent will be obtained.

Detailed history of past medical/surgical illness will be obtained.

Routine investigations will be done preoperatively.

Anesthetic technique:

Baseline demographic parameters, blood pressure, and heart and respiratory rates will be recorded.

Standard monitors: electrocardiogram, pulse oximetry, Invasive blood pressure monitoring, CVP monitoring, ETCO2 after intubation.

Peripheral venous access will be obtained with 18G venflon.

Epidural catheter will be inserted between the thoracic level d10/11 vertebral interspaces and after performing a test for correct extradural placement, a dose of morphine 4mg in 10 ml saline solution will be administered.

Left Radial artery cannulated and blood pressure will be recorded after connecting to transducer zeroed at mid-axillary level.

Anesthesia will then be induced using propofol 2 mg/kg in combination with fentanyl 2 ug/kg. Tracheal intubation will be facilitated by neuromuscular relaxation atracurium 0.5mg/kg. Anesthesia will be maintained with volatile anesthetics (sevoflurane) in N_2O and O_2 mixture .

A central venous catheter will be inserted via internal jugular vein and central venous pressure recorded. Sufficient analgesia will be provided using 20 ug boluses of fentanyl.

All patients will be mechanically ventilated with tidal volume 8 ml/kg and positive end-expiratory pressure (PEEP) 5, respiratory rate 12 to maintain normocapnia.

Hemodynamic monitoring:

Before induction of anesthesia, an arterial line will be inserted into the radial artery of the non-dominant forearm and first measurements recorded.
Optimal pressure signal damping will be assessed using flush test before the first measurements. Vigileo/FloTrac device (Edwards Lifesciences, Irvine, CA, USA) with software version 1.10 will be used for measuring Stroke volume variation(SVV) and other hemodynamic variables like CI, Stroke volume index
After anesthesia induction and before the beginning of surgery, an 8F central venous catheter will be inserted in the right internal jugular vein. Central venous pressure (CVP) will be continuously measured by using a transducer calibrated to the mid axillary level.Cardiac index(CI), Systolic blood pressure(SBP),Heart rate(HR),Stroke volume(SV), and Stroke volume variation(SVV) will be continuously measured.

Protocol:

After induction all patients will be maintained on Ringer lactate based on 4-2-1 formula. Half an hour after induction a first volume loading step will be performed with 100 mL of colloid solution (6% hydroxyethylstarch) for 2 min in the peripheral IV line. Hemodynamic variables will be recorded prior to the administration of the volume loading step. The hemodynamic variables will be recorded again 1 min after the end of the infusion. The volume loading step (VLS) will be termed

- **Responsive VLS** when there was an increase in stroke volume SV by at least 5%
- **Nonresponsive VLS** when there was no change or the increase in stroke volume SV was less than 5%.

Volume loading steps will be conducted every 30 minutes after the first VLS. Each patient will undergo multiple volume loading steps every thirty minutes until three responsive and three non responsive volume loading steps are obtained. Six volume loading steps three responsive and three non responsive will be obtained from each patient and will be analysed. In each patient, When a volume loading step is responsive another VLSs will be performed until a nonresponsive VLS is reached.

Analysis

All hemodynamic variables were analyzed as continuous variables and expressed as the mean ± SD.

To determine whether hemodynamic variables changed in relation to volume loading, differences between values before and after each VLS were compared between responsive and nonresponsive VLSs by using a two-tailed *t*-test.

The correlation between changes in SV and changes in hemodynamic variables was assessed by using Pearson's correlation.

To assess the ability of different hemodynamic variables to discriminate between positive (>5% increase in SV) and negative (<5% increase in SV) response to fluid challenge, receiver operating characteristic (ROC) curves were generated for HR, SBP, CVP, and SVV, varying the discriminating threshold of each variable.

The area under the ROC curve for each variable was calculated and compared. Values for each area can be between 0 and 1. A value of 0.5 indicates that the screening measure is no better than chance, whereas a value of 1 implies perfect performance. In our study, the area under the ROC curve represented the probability that a random pair of responsive and nonresponsive VLSs would be correctly ranked by the hemodynamic variable measurement.

REFEERENCES:

1.Berkenstadt Haim, Nevo Margalit,Moshe Hadani Stroke volume variation predictor of fluid responsiveness in brain surgery patients.Anesth Analg 2001;92:984-9.
2.Hofer CK, Senn A, Weibel L, Zollinger A. Assessment of stroke volume variation for prediction of fluid responsiveness using the modified FloTrac and PiCCOplus system. Crit Care. 2008;12:R82. doi: 10.1186/cc6933
3.Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds RM, Bennet ED. Early goal-directed therapy after major surgery reduces complications and hospital stay. A randomised, controlled trial. Crit Care. 2005;9:R687–R693. doi: 10.1186/cc3887.
4.Chest 2008 Jul;134(1):172-8.Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares.Marik PE, Baram M, Vahid B.
5.H. Liu, M. Konia, Z. Li & N. Fleming : The Comparison of Stroke Volume Variation and Arterial Pressure Based Cardiac Output with Standard Hemodynamic Measurements during Cardiac Surgery. *The Internet Journal of Anesthesiology.* 2010 Volume 22 Number 2.
6.Kumar A, Anel R, Bunnell E, Habet K, Zanotti S, Marshall S, Neumann A, Ali A, Cheang M, Kavinsky C, Parrillo JE. Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. Crit. Care Med. 2004;32: 691-99
7. Manecke GR. Edwards FloTrac sensor and Vigileo monitor: easy, accurate, reliable cardiac output assessment using the arterial pulse wave. Expert Rev. med. Devices 2005; 2(5):523-27
8.Manecke GR. Cardiac output from the arterial catheter: deceptively simple. J Cardiothorac Vasc Anesth. 2007;21:629–631. doi: 10.1053/j.jvca.2007.07.001.
9. Prasser C, Trabold B, Schwab A, Keyl C, Ziegler S, Wiesenack C. Evaluation of an improved algorithm for arterial pressure-based cardiac output assessment

without external calibration. Intensive Care Med. 2007;33:2223–2225. doi: 10.1007/s00134-007-0859-9.
10. Lopes MR, Oliveira MA, Pereira VO, Lemos IP, Auler JO Jr, Michard F. Goal-directed fluid management based on pulse pressure variation monitoring during high-risk surgery: a pilot randomized controlled trial. Crit Care. 2007;11:R100. doi: 10.1186/cc6117.